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BANQUET PROGRAM

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Maitland, Fla.

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(6) Etiology of Uterine Flexures With the Proper Mode of Treatment Indicated.
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(1) Dr. William Goodell, Philadelphia, Pa.   Dr. Robert A. Kimbrough, Jr.,
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(5) Dr. J. Marion Sims, New York City   Dr. Emil Novak,
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The AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY is proud to present in this special commemorative issue the Proceedings of the Seventy-fifth Anniversary Meeting of the American Gynecological Society and to recall that, with its predecessor, it has had this honor during the entire period of the Society's existence. The American Gynecological Society is believed to be the first national organization in the world devoting itself to this special field of medicine and has witnessed the almost revolutionary changes which have taken place, not only in gynecology and obstetrics, but in all domains of medical practice. Yet it is of interest to observe that certain of the topics presented in the Anniversary program at the Banquet remain topics of discussion even at this advanced day and age.

To the Society, for which the JOURNAL has continued to be the official organ of publication during these many years, the Editors and Publishers desire to extend herewith their appreciation of this relationship and their felicitations for its continued welfare.

PROLOGUE

FRED L. ADAIR, M.D., MAITLAND, FLA.

NOW that the postprandial somnolence is creeping over you, dreams can carry you back three-quarters of a century to scenes of lesser dimensions when the same problems both great and small will be before your minds.

Then as now the processes of reconstruction, for the preservation of human rights and liberties, by physical, mental, and moral forces were at work.

Among these movements was one which in a small way represented the determination of scientific minds to further human progress, health, and welfare.

The incentive for the formation of our Society emanated from two great centers intimately associated with the origins, the destructive and constructive forces, and the material, scientific, and moral decline and regeneration of our country and its varied activities. On May 24, 75 years ago, following various conversations and consultations, a summons was sent to a number of leading specialists, which resulted in an organizational meeting. This session was held in the Hoosak Hall of the New York Academy of Medicine on June 3, 1876. Some 20 founders are listed in the archives and officers were elected. You will meet the then Chairman as a participant on the program of the evening. He was a New Yorker. The original Clerk will also participate in this evening's memorial. The elected Clerk was from Boston but other sections were represented in an official capacity.

None of the Founders are now living and of the many officers there are 11 presidential survivors, 27 vice-presidential, among the much larger number of prior incumbents. Among the smaller number of secretaries, 11 survive and 6 treasurers are still among us.

These men must have envisioned a greater Boston arising from the ashes of a great fire with its splendid educational and other institutions among which would be those devoted to the care of women and to progress in the fields of education and investigation. Also the leaders from New York must have realized the tremendous potentialities of their city as it threw off the corruption of Tweedism. Among our founders were those who established enduring institutions which, in spite of human frailties, conflicting ambition, and misunderstandings, have come to be among the leading institutions of the world.

We can imagine James Read Chadwick, a Harvard medical graduate of five years, stating in impressive words the future plans of this society. We cannot duplicate his voice but his words read: "Gentlemen: The call, to which you have responded by your presence here today, was addressed to a limited number of recognized gynecologists, after consultation with several of the prominent men of Boston, New York, Philadelphia and of the West. It was not intended to include all those whose labors in this field of medicine so fully entitled them to an honored place in our ranks, but simply to form a nucleus around which the gynecologists of the country should cluster.

"With regard to the special plan under which we should organize, it has been generally conceded to be better for our Society to have a restricted membership and to require high qualification in the candidates for admission. By this means membership will come to be coveted and our discussions be more profitable."

The Chairman of this meeting, Edmund Randolph Peaslee, physiologist, anatomist, pathologist, gynecologist and obstetrician, originated in Massachusetts, developed in Connecticut and elsewhere, and came to fruition in New York. His remarks forecast a brilliant future for the society, stating, "I will confess that I have been surprised to see such a number of representative men brought together, for this purpose, from far and distant cities and while I heartily approved of the formation of a national society, which should have for its object the promotion of knowledge in all that relates to the diseases of women and to obstetrics, I must make the humiliating confession that, in my inmost heart, I did not give my brethren who have, at such cost and sacrifice of time, come to this city for this purpose, the credit for such zeal and devotion to that department of science, to which they have dedicated their lives, as this gathering demonstrates. This is assuredly a most favorable augury for the future of this society."

The Council, which was elected at this organizational meeting, met immediately after adjournment and set a time for the first annual meeting and appointed a committee to arrange the program. The place of the meeting was to be in this city and the dates were Sept. 13-15, 1876.

The meeting was held as scheduled at which time the constitution and bylaws were adopted which provided among other things for annual dues of ten dollars.

Now while the dollar is smaller the field of obstetrics and gynecology has expanded so tremendously that it is difficult for us to place ourselves in the position of these great pioneers who manifested such acumen, ability, and vision. Lister, Virchow, and Pasteur were in their prime, but Roentgen was 20 years away, and the radioactivity of the Curies was even more remote.

The so-called ductless glands were closed books and the complexities of the human blood were for the most part not understood. The maternal and fetal physiology and pathology were little comprehended except from a mechanical point of view. The psychiatrists had not yet explained why we act like human beings.

The founders of our society not only organized our American Gynecological Society but were catalysts in their own communities, stimulating far-reaching ideas and plans which have resulted in untold benefits to the medical profession, our specialties, and above all to humanity.

You are being projected back 75 years to meet some of the outstanding physicians who contributed to the program of the first scientific session of this society. You are now being transported to Hoosak Hall at the New York Academy of Medicine, in the year 1876.

You will see and hear from the Presiding Officer of the first session and others who will be presented by the first President of our Society, Dr. Fordyce Barker of old New York.

THE MEETING AS PORTRAYED BY MEMBERS OF THE
PRESENT DAY*

DR. FORDYCE BARKER†.—Fellows of the Society and Guests, Ladies and Gentlemen, the first Annual Meeting of the American Gynecological Society will please come to order. This Society has been founded for the promotion of knowledge in all that relates to the diseases of women and obstetrics. It is our earnest hope that the ensuing years will find this object accomplished to the benefit of Medicine and to the credit of our Fellows.

THE ETIOLOGY OF UTERINE FLEXURES, WITH THE PROPER
MODE OF TREATMENT INDICATED

Thomas Addis Emmet, M.D.,‡ New York, N. Y.

M R. PRESIDENT: My purpose in presenting to this Society the etiology of uterine flexures for discussion is with the hope that it may be the means of establishing for our guidance the proper mode of treatment. Certainly much good must result from a full consideration of this subject; for, with the united experience of this body, the true course which a conscientious man should follow will be pointed out. Let us have the views and experience of those who have relied chiefly on the use of the knife; and, on the other hand, the mode of treatment from those who deprecate all surgical interference.

There are certain cases where the aid of surgical means has, beyond question, accomplished much, and where the surgeon would have failed in his duty had he neglected to give his patient its benefit. Other conditions have existed where a resort to the knife would have been malpractice, and it was proper to employ other means of treatment.

I have attempted with great care to analyze the records of three hundred forty-five cases of different forms of flexures which have been treated in my private hospital.

The forms of flexure will be treated of in the following order: Of the cervix, at or below the vaginal junction, and of the body, forward, backward, and lateral, the last being probably but deviations from the other two forms of the body. Retroflexions are comparatively rare. The relative frequency of retroflexures to the number of anteflexures is very nearly in the proportion of one to three. Quite different is the proportion for version of the uterus, since the posterior position is as frequently found, if it be not even the more common.

Painful menstruation is, from its character, an indication of the form of flexure. Thus we see, with flexures of the cervix, pain at the beginning of the flow is the rule and during the flow the exception. Thus all women suffered pain during the flow, showing this to be the rule, while pain at the beginning of the flow is the exception, in anteflexures of the body. The existence of flexures of the cervix is before the time of puberty, those of the body are formed in after life.

So that in flexure of the cervix, the most numerous class of all, a condition of puberty and early life, relief is sought at the earliest age; anteflexures of the body follow soon after, while retroflexures and the lateral ones, being less common and found in about the same proportion, are developed in later life.

Anteflexures may arise from means taken to prevent conception in early married life by the sterile, and by those who had already borne children; many ill-assorted marriages; and mental disquietude.

Flexures of the cervix have their origin at about the age of puberty by the balance being lost between the relative growth of the body and cervix. From the earliest development of the uterus until pregnancy some degree of ante-version exists as a rule. With the uterus in this position the neck cannot be developed to an undue length without forcing the cervix forward in the axis of the vagina where the least resistance is offered. As the body lies forward, the cervix must become bent upon itself at, or near, the vaginal junction, and thus the flexure is formed.

The rule as regards pain is that it exists previously to the appearance of the flow, and then ceases, or becomes much less. If the degree of flexure is slight, there may be an absence of pain, or the pain may not come on until after the flow has become fully established.

I am unable to recall any other condition where menstruation, being painful at the beginning, is relieved so promptly when the flow becomes established. This may therefore be regarded as a characteristic symptom of a simple un-complicated flexure of the cervix.

Retroflexions of the body are, I believe, deviations from a previously exist-ing retroversion. While they are always aggravated by an obstructed circula-tion, as in the case of other flexures of the uterine body, the exciting cause is inflammatory action, not in the organ itself but in the connective tissue of the pelvis and ligaments of the uterus. From a moment's reflection it will be evi-dent that the uterus may be retroverted to a point at which the broad ligaments, being already on the stretch, may by inflammation become shortened so as to produce the flexure. This action may be also aided, with shortening of the broad ligaments, by inflammation in the uterosacral ligaments. When a point in the version has been reached at which the anterior wall of the vagina can no longer yield to the upward pressure of the cervix, any contraction of these liga-ments will increase the degree of retroflexion. Since inflammation of the neigh-boring cellular tissue of the pelvis is, I believe, almost always, if not invariably, an accompaniment of retroflexion, these ligaments become necessarily more or less involved.

In 1865 I stated, "A large hospital experience led Dr. Sims, some years ago, to abandon all methods as unsafe and negative in result, for the relief of this condition, except the incision of the neck as proposed by Professor Simpson. My experience has fully corroborated his teaching; we agree perfectly in principle, and only differ in the method by which it should be done. His ingenuity suggested an incision of the posterior lip directly backward in the median line; but after a few operations he abandoned this method as unsatisfactory. By subsequent observation of these cases, I satisfied myself that they could not be permanently relieved by either operation, as the seat of difficulty was entirely above the point reached by the incision." "I am satisfied that neither operation will permanently relieve any case unless the flexure is confined to the neck and is below the vaginal junction. While the backward operation, as proposed, would relieve a moderate flexure, the lateral one, however, even if extended on each side to the vaginal junction, could not accomplish so much, unless the posterior flap, in the process of healing, retracted sufficiently to clear the seat of stricture, which it could not do. The dysmenorrhea invariably returns after a few months, as soon as the mere revulsive effects of the operation have subsided."

"I have for several years in this, as in all other operations of obstetrical surgery, substituted, as far as possible, the use of the scissors for the knife. Although they may be deemed less surgical, I have satisfied myself that I can operate more rapidly, and certainly have experienced less hemorrhage with them. The scissors that I have been in the habit of using for this operation are flat on the face, but have blades curved at an angle from the handles, so as to conform somewhat to the direction of the uterine canal. Simpson's uterotome is not applicable to this operation and cannot be used except where the canal is straight. Dr. Sims introduced an instrument having a narrow cimeter-shaped blade, about an inch and a half in length, which answered admirably for the purpose; but having a single joint, the blade can only move in the one plane and to cut in the opposite direction it is necessary to have a second instrument with the reverse. This difficulty led me several years ago to have an instrument made with the same shaped blade but terminating in a ball at the seat of the joint and separate from the instrument. The handle, being contrived like a pair of forceps, grasps the blade firmly in a socket at the required angle. It being, in fact, a universal or ball and socket joint, the blade may be used in any direction and it is a valuable instrument for other purposes."

"Formerly, I divided the anterior lip in the median line for the relief of dysmenorrhea depending upon retroflexion, and at least in theory, the operation seemed quite as applicable as the other one in anteflexion; but I have long since abandoned the operation. I have had, to my sorrow, pelvic cellulitis with abscesses frequently occur, and death in one instance, after the most careful preparatory treatment previous to operating, when, at the time, there was not the slightest indication of danger. In fact I am unable to recall a single instance where inflammatory symptoms did not occur if an attempt was persevered in to keep open the incision while the uterus remained in this position. Retroflexion, however, can be cured by the long-continued use of hot water injections

and hot baths, blistering the neck occasionally to deplete by the watery discharge, daily glycerine dressing, and by a careful attention to the state of the bowels and general condition.

"For the relief of the flexure at the vaginal junction, I always divide, with scissors, the posterior lip backward in the median line. This operation is attended with but little risk, if the case is properly cared for, from the fact that the organ is otherwise in a comparatively healthy condition; unless the history of the case points to the existence of a previous attack of cellulitis, resulting from some accidental cause, there will be but little danger of this complication from the operation. Quite the contrary will be the case when the body has been involved in either anteflexion or retroflexion of long standing, for a certain amount of perimetritis is almost certain to have existed at some previous date, leaving a condition afterward requiring but a slight provocation to re-establish the inflammation in a more serious form. Although there may be no bleeding at the time of operation, the use of a tampon for some ten days is a necessary precaution to guard against subsequent hemorrhage.

"During the time I held the position of surgeon-in-chief to the Woman's Hospital, from September 1, 1862, to May 1, 1872, this operation was performed sixty times in the institution. During the year 1870 four lateral operations were performed for the removal of fibroids, making a total of fifty-six operations for flexure of the cervix."

"Three cases of serious cellulitis followed these operations, but from which complete recovery took place; one death occurred from general peritonitis, coming on after the patient was well enough to be up, and it could be attributable alone to her own imprudence."

It is my rule never to operate until a patient has been sufficiently long under observation for me to appreciate fully her condition and to prepare her properly for the operation. The pelvic abscess, following an attack of cellulitis, was brought about by the patient's imprudence in sitting up and exposing herself to cold in a nightdress and bare feet.

A death followed a division of the cervix by me, and took place several weeks after the patient had passed from my charge in May, 1872. It was, I believe, about three weeks after the operation, when out for the first time, that, after a long ride, she was attacked with peritonitis, and died.

The treatment of flexures of the cervix may be narrowed down to the use of surgical means, if the flexure is well marked, since we have no better agent for rectifying the condition. We must however be certain that no tendency to cellulitis exists, and that the patient is in a proper condition for the operation.

For flexures of the body, the rule of practice is to be reversed, since no operation can be of the slightest benefit, so long as the condition exists which caused the flexure. An operation will generally prove a detriment to the patient's condition afterward, and is frequently the indirect cause of death as we all know.

In the local treatment of flexures of the body, we must be governed by the same general principles as are applicable to any other form of uterine disease. The chief reliance for giving tone to the pelvic vessels and for removing the

chronic state of venous saturation, as it were, lies in the proper use of the hot water vaginal injections, at a temperature of from 100 to 110° in accordance with the urgency of the case.

After thus stating my own views, and experience to so great a length, with but the single purpose in view, I trust that I may be instrumental in drawing out the opinions of others on this subject for our common benefit.

Of course, if there do be among you those who do not believe as I do, I might answer in the words of a Catholic priest I know of. He was a great friend of John Wesley. Wesley vigorously disputed with him, saying he did not believe in purgatory. Whereat the priest retorted, "Ah well, John, you might go farther, and fare worse."

Discussion of Dr. Emmet's Paper
By Dr. Peaslee*

Mr. President:

Before discussing Dr. Emmet's paper I think it would be appropriate to give a little of his background and detail the source of the vast material from which he gleaned his information. I shall quote as he has written in the preface of the first edition of his book which is to be published soon.

"From 1862 to 1872 at the Woman's Hospital of the State of New York I was the surgeon-in-chief, with entire medical control and sole responsibility in the treatment of its inmates.

"In the beginning the capacity of the hospital did not exceed that of an ordinary-sized dwelling. Later a handsome edifice was built under my personal supervision, organized by myself, and brought to a high state of prosperity before any change was made in its management. Up to the date of the reorganization in 1872 about three-fourths of all the patients admitted had been under my care, and I had performed even a larger proportion of the surgical operations. To the enormous clinical advantages thus available have been added those of my private hospital, now in operation sixteen years, and those of an extensive consulting practice."

Dr. Emmet, a gentleman who, according to his own words, and I quote—"excludes *rigorously* what he knows to be erroneous in precept or practice," has presented his views to us on the subject of uterine flexures.

The author modestly submits and describes the correct treatment of anteflexure as complete discission of the posterior cervix. What he really is describing is an operation to relieve cervical stenosis. For this latter condition I have developed an operation which I have called "superficial trachelotomy" and which is preferable to complete discission of the cervix. It is the cervical stenosis that results in the production of symptoms rather than the flexure of the uterus as contended by Dr. Emmet. Accordingly he has had success in treating these patients. He did not alleviate the flexure but he did correct the stenosis. Again I would mention that superficial incision or even simple dilatation will accomplish the purpose in a much more satisfactory and safe manner.

*Dr. John I. Brewer, Chicago, Ill.

EXTIRPATION OF THE FUNCTIONALLY ACTIVE OVARIES FOR THE REMEDY OF OTHERWISE INCURABLE DISEASES

ROBERT BATTEY, M.D.,* ROME, GA.

SOME four years ago I brought to the notice of the medical profession, through the columns of the *Atlanta Medical and Surgical Journal*, a new surgical operation and related a case in which I had removed the ovaries, still in a state of functional activity, from a young lady who was suffering serious detriment of her health and peril to her life by reason of an excessive menstrual molimen which was wholly unrelieved by the usual menstrual flux. In the intervening time other similar operations have been performed. In scarce any two cases of the short series have the urgent symptoms complained of been the same or strikingly analogous and yet all have had certain features in common, which may very properly group them into a single class in as much as they have all been characterized by a vicious or abnormal ovulation upon the one hand, and have all obstinately resisted the more usual and well-accepted methods of treatment upon the other hand.

I am very sensible of the fact that the number of these operations is as yet entirely too small to establish any new principle or warrant the drawing of any definite conclusions from the facts thus far ascertained. My own inclination would be not to intrude either my work or myself upon the notice of my brethren until I might be able, at a future time, to offer more enlarged and more mature results. Two considerations, however, have prevailed with me to make to the Society this meager report, namely: an expressed desire of certain members of the Society to have early possession of the facts thus far ascertained and the consciousness that my obscure and circumstribed field of labor must necessarily render the accumulation of additional facts very slow and difficult in the future as it has been in the past.

In doing these operations I have sought to effect a cure of the varied maladies complained of by the removal, in certain instances, of an ovary viciously or abnormally performing its functions and more frequently by the removal of both ovaries, to put an end to ovulation entirely, and thus to determine the menopause or change of life, whereby I have hoped, through the intervention of the great nervous revolution which ordinarily accompanies the climacteric, to uproot and remove serious sexual disorders and re-establish the general health. I have done ten operations in all.

The patients' ages varied from 24 years to 38 years. Both ovaries were removed from 7 patients and only one ovary from 3 patients.

The symptoms and complaints in all were severe and compelling. A few or many of the following were present; convulsions, excessive menstrual

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molimen, mania, neuralgia of the ovary, morphia addiction, pain, dysmenor-rhea, coccydynia, hysteria, vomiting, decubitus, and epilepsy.

My first operation was through the abdominal wall, all the others through the cul-de-sac, with the patient on her left side in a semiprone position. The latter method presents several advantages, all of which are known to you.

Silk ligatures were employed to bring the ovaries into view, but seldom for hemostasis. The écraseur, scoop, and the true tactus eruditus control bleed-ing, allow complete removal, and prevent injury to adjacent tissue.

There were 2 deaths in this series. The first patient died on the tenth postoperative day after a febrile course. Autopsy revealed an abscess about the ligature on the right, which abscess had ruptured into the general perito-neal cavity with resulting peritonitis. Perhaps early drainage with a catheter or peritoneal irrigation using Peaslee's method might have been lifesaving.

The second patient had a rapid pulse and myocardial weakness. She re-quired some days for preparation. Death occurred on the third postoperative day. Though she was febrile the picture was primarily one of circulatory collapse. Autopsy was denied us.

The term *normal ovariotomy,* which I adopted for my original operation has received at the hands of the profession almost universal condemnation. I confess myself still too obtuse to see clearly the appositeness of the general criticism which has been made upon me by my use of this term.

When I extirpate an ovary which, although it may be diseased, is easily and distinctly recognizable as an ovary, and which is regularly performing its function as an ovary I feel that I am doing the operation of ovariotomy nor-mally, or, in other words, that I am doing *normal ovariotomy.* When either of my friends around me is engaged in the extirpation of a huge and unsightly tumor from the abdomen of a woman, a tumor in which I can recognize no form or semblance of an ovary whatever, I feel that the operation is abnormal ovariotomy.

What are the indications for this operation? I have endeavored to make myself understood in answer to this question in my published communications and reports but I regret to say with little success. When I report a case of amenorrhea, it is commented upon as dysmenorrhea; when I assert that I do not operate for nymphomania, and that the removal of the ovaries does not annul the aphrodisiac propensity, it is boldly stated in criticism, that I do op-erate for nymphomania, and that the operation is a failure.

In my opinion the removal of the functionally active ovaries is indicated in the case of any grave disease which is either dangerous to life or destructive of health and happiness, which is incurable by other and less radical means, and which we may reasonably expect to remove by the arrest of ovulation or change of life. I do not propose it for any case which is curable by other means.

Should one or both ovaries be removed? When we consider the grave character of the cases in which these operations are done; when we consider

the difficulties which attend upon a second operation; when we consider the proneness of the ovary left behind to become the seat of disease; and when we take into account the advantages which we may expect to gain by the alterative results which attend upon the change of life, it may well be asked if the necessity which condemns the one ovary ought not to condemn the other also.

The complications which may be encountered are: adhesions, which are sometimes extensive and intimate; indeed, the ovary may be so buried in lymph as to render its recognition difficult, as in Case 4, where even the erudite touch of Dr. Marion Sims did not determine the point fully, and it was only rendered clear by bringing away portions of the ovary itself with my fingernail.

Hemorrhage has never been troublesome in any case; generally the loss of blood has been very trifling. I attribute this exemption to the fact that I move the écraseur chain very slowly and give ample time for hemostasis. In one instance where there was rather free venous oozing I stopped it quickly by pushing small lumps of ice into Douglas' fossa; these melted and the water drained away at once. The fact should not be overlooked that there might be troublesome hemorrhage in this operation.

Of the aftertreatment little is to be said. In general it has been sufficiently simple. In two or three instances I have found it necessary to wash out the cavity with a double-current catheter, in the others only syringing the vagina has been required.

Discussion of Dr. Battey's Paper by Dr. William Goodell*

Mr. President, Fellows of the American Gynecological Society, Distinguished Guests, Ladies and Gentlemen:

At this first meeting of our new society it is indeed regrettable that I must disagree so emphatically with practically every remark made by our distinguished colleague from Georgia. I sincerely trust that the vehemence of my discussion will not be taken by him as a personal affront—a circumstance which would be most unfortunate in view of the fact that but eleven years have elapsed since the cessation of hostilities between our respective sections of this now united nation.

In my opinion there are only two indications for the removal of normally functioning ovaries: first, for control of excessive bleeding of fibromyomas, and, second, for the relief of pain incident to incarceration of the ovaries in the cul-de-sac of Douglas.

A review of the ten cases cited by Dr. Battey discloses an absurdly wide variety of conditions which he so lightly designates as "otherwise incurable diseases." That extirpation of one or both ovaries cannot be expected to remedy such conditions as epilepsy, mania, hysteria, and neuralgia is more than adequately proved by his admission of poor results in seven of the ten cases which he has reported.

Dr. Battey's rationale for the performance of his operation is that of establishing the menopause by removal of both ovaries. The ovular theory of menstruation, while attractive in many of its aspects, has by no means been proved. Certainly the evidence cited by the essayist is far from convincing: in three cases but one ovary was removed; two other patients died; of the remaining five, two cases were so complicated by adhesions that total extirpation was impossible; of the three in which removal of both ovaries was accomplished,

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two ceased to menstruate; the third patient, while relieved of her convulsions, is now subject to recurrent uterine hemorrhages which continue unabated for two to five weeks.

Concerning the method of the operation, I find myself in agreement with Dr. Peaslee in preferring the abdominal to the vaginal approach. Because of the difficulties offered by adhesions and the danger of hidden hemorrhage, I prefer to see what I am doing.

If I may be forgiven an attempt at prophecy, I dare say that eventually the ovaries will be found to elaborate substances which will tend to alleviate the very symptoms for the relief of which Dr. Battey now advocates their removal.

For many reasons, including the high mortality rate, I have not yet performed this illogical operation, and, if any of my associates in the University of Pennsylvania should become a follower of our colleague from Georgia, his immediate resignation will be requested.

Mr. President, I thank you for your indulgence.

LABOR COMPLICATED BY UTERINE FIBROIDS AND PLACENTA PREVIA

JAMES CHADWICK, M.D.,* BOSTON, MASS.

MRS. M. M. came to me on May 12, 1875. She was 42 years of age, had been a widow for two years. A tumor had been diagnosticated 5 years previously. Menstruation had been excessive and metrorrhagiae frequent. The growth at the navel was 34¼ inches, and midway between the navel and the pubes was 35¾ inches. Palpation showed that the abdomen was the seat of a large tumor. The vagina was unduly moist, and its roof less yielding than usual. The diagnosis of uterine fibroids seemed unequivocal.

I told the patient to call again in a week, when I could begin treatment by subcutaneous injection of ergotine.

On May 17, I had the syringe charged, when something led me to examine the abdomen again with care. Flatness extended over the greater part of the left side of the abdomen. Nodules could be felt only by deep pressure. Fluid alone could produce the flatness. Pregnancy flashed into my mind as the only condition that could explain the phenomenon satisfactorily, and this suspicion the stethoscope confirmed by the discovery of the fetal heart sounds two inches below the umbilicus. It is needless to add that the nodules in the left side were the feet. A hemorrhage within two weeks caused me to suspect the presence of a placenta previa as a further complication.

Further questioning elicited the facts that coitus had taken place but three times since her husband's death. Sterility during thirteen years of married life, and the belief that her age—42 years—fully accounted for the derangement of menstruation, had prevented any suspicion of the real fact having entered the mind of the patient. On learning the truth, she fell into a state of utter despondency, which persisted to the end, and exercised a very appreciable influence in determining the results.

Mrs. M. passed to the full term of pregnancy without other untoward events than several smart hemorrhages, requiring only repose in bed for their arrest. On August 13, the uterus began to contract feebly, but with some regularity. Hemorrhage set in, and soon assumed alarming proportions; it was checked by plugging the vagina with a Barnes' dilator.

After consultation with Drs. A. D. Sinclair and E. G. Cutler, of Boston, ether was administered, and the cervix gradually dilated by digital pressure and manipulation. The placenta was previa, but luckily only its border covered the os. It was found to have its seat immediately over a large fibroid, in the posterior uterine wall, that descended to the internal os, and proved a serious obstacle to the insertion of the hand. This was, however, at last, effected, the feet seized and dragged down. The greatest traction that I dared

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apply only brought the knees to the vulva. With the exercise of great care, yet considerable force, I insinuated a hand along the curve of the sacrum, between the abdomen of the child and the fibroid tumor; with great difficulty grasped one arm after another, and brought them into the vagina, fracturing the right clavicle during the process. By continuous forcible traction the shoulders were finally delivered, though the head evidently remained above the brim of the pelvis.

Again and again I tugged upon the body, while Dr. Sinclair pressed the head down from above the pubes. At length it descended suddenly into the pelvis and was at once delivered.

The child was asphyxiated but revived after fifteen minutes, during which artificial respiration was kept up. He weighed ten pounds.

The placenta not coming away, and there being no expulsive efforts of the uterus, the former was removed in a somewhat torn condition by the hand. In order to make sure that no portion had been left, I introduced by hand into the vagina, and to my dismay felt it pass into the peritoneal cavity outside of the uterus. Above the fundus of the uterus could be felt the intestines, but they showed no tendency to descend into the pelvis. A careful examination of the rent by Dr. Sinclair and myself made evident that it was a transverse tear of the vagina, three or more inches in length, situated just below the insertion of the vagina into the posterior lip of the uterus. Just above this lip, it will be remembered, was the large fibroid which had obstructed delivery.

There seemed to be no hemorrhage, so the ether was removed, the woman turned upon her back, and a tight bandage applied, by which means it was hoped that the edges of the wound would be kept in apposition, owing to the pressure of the uterus.

It is useless to give the subsequent history in detail. The first day was passed in perfect comfort; on the second, symptoms of peritonitis began to appear. On the third day, the abdominal distention was so great as to require puncture of the intestines to allow the escape of flatus. Through the same trocar, I essayed the injection of nutrient and stimulant fluids into the intestinal canal. The feasibility and objects of this procedure were fully set forth in a paper which I read before the New York Obstetrical Society on November 2, 1875. On the fourth day, septicemia and delirium set in, terminating fatally on the fifth day.

No autopsy could be obtained.

Several points in this case seem to merit consideration.

I saw one year ago a similar case. Mrs. F. M., 33 years of age, had been married fifteen years without having had children or miscarriages. Menstruation had always been regular until seven months previously; since then, it had not been seen.

After two months of amenorrhea, one of the most eminent and trustworthy physicians of Boston noted nothing abnormal, except that the cervix was "hard, red and granular," almost exciting a fear of commencing cancer.

Four months later, one of our most prominent ovariotomists, finding several large abdominal tumors, gave an unfavorable prognosis. One month later, the seventh without menstruation, it required no great acumen on our part to recognize advanced pregnancy, complicated by a fibroid tumor larger than a man's fist in the anterior uterine wall. At term, the patient was delivered safely by Dr. Kingsbury; at the end of another month, I was unable to find any trace of the fibroid.

I have been able to collect only seven additional instances of labor complicated with uterine fibroids and placenta previa. They are given in detail in the version of my discourse submitted for publication in the *Transactions* of this Society.

The problem naturally presents itself: what course should be pursued when a fibroid tumor is recognized in the pelvis, and likely to interfere with delivery? If seen early enough in the pregnancy, the induction of miscarriage or premature labor would probably be attended by less risk than any other course. If the pregnancy be too far advanced to allow a reasonable chance of the passage of the fetus past the obstruction, then version, and reduction of the size of the head by the trephine, or the cephalotribe, would commend itself to my judgment. I would not perform cesarean section unless the obstructing tumor almost filled the pelvis. The same rules should govern practice, as in obstruction of the pelvis from other causes, except that enucleation of the tumor might in rare instances be feasible in spite of its manifest dangers.

Discussion of Dr. Chadwick's Paper by Dr. A. J. C. Skene*

Mr. President, Fellows and Guests:

Mine is a most difficult assignment. My esteemed colleague from Boston, for whom I have the utmost personal admiration, has given us the harrowing details of a first pregnancy in a 42-year-old widow who died of septicemia after a most difficult confinement.

It was my privilege to read the entire manuscript with its many comparable case records. The essayist's erudition is indicated by the fact that these case reports were gleaned from the world of literature, English, German, French, and Austrian.

Mr. President, if I interpret the objectives of this newborn Society correctly, it then behooves me to subject this report to critical analysis rather than to indulge in fulsome praise and commiseration.

Dr. Chadwick reached his diagnosis in its entirety on May 17 of last year, the pregnancy then being of 6 months' duration, complicated by a blocking fibroid and a suspect placenta previa.

In a thoughtful analysis of the safest treatment for pregnancy of varying duration, complicated by a blocking fibroid, the essayist recommends induction of miscarriage or of premature labor if the patient is seen early enough.

This was not done here.

Thereafter at term, August 13, the lady entered into desultory labor. During the next 24 hours the patient at one time bled so much that the vagina was plugged with a Barnes colpeurynter. Dilatation of the cervix never passed beyond 1 finger. Eventually accouchement forcé was decided upon and carried out by digital and manual dilatation of the cervix, version and extraction, and manual removal of the previa placenta.

The details of this delivery and the unfortunate aftermath have been described in great detail by Dr. Chadwick.

*Dr. Ralph Ries, Chicago, Ill.

Here again the essayist in his most excellent analysis urges collapse of the aftercoming head by trephine or cephalotribe as a lifesaving device for the unfortunate parturient.

This was not done.

Dr. Chadwick quotes a somewhat similar case treated successfully by cesarean section by Dr. Cazin, in Boulogne in 1874.

This was not done.

The cause of the avulsion of the posterior vaginal wall from the cervix is discussed in great detail. Two possible explanations of this disaster are offered: (1) the great difficulty encountered in insinuating the hand between the fetal abdomen and the posterior wall fibroid in order to reach and deliver the arms; (2) the prolonged and vigorous pull from below and push from above which resulted finally in an abrupt descent of the aftercoming head.

I submit that this theorizing is largely academic.

The incontrovertible fact remains that the avulsion was due to the exhibition of unusual force.

Gentlemen, how well we know the strain upon us when a life or two lives are at stake. "Let him who is without sin cast the first stone." I am sure that my friend Dr. Chadwick and all of you will forgive this critical analysis and accept or refute it according to your own lights.

It remains only for me to emphasize once again the age-old injunction applicable to all operators: "Non vi, sed arte."

Thank you.

LATENT GONORRHEA, ESPECIALLY WITH REGARD TO ITS INFLUENCE ON FERTILITY IN WOMEN

EMIL NOEGGERATH, M.D.,* NEW YORK, N. Y.

WHEN I presented my monograph on latent gonorrhea in Hamburg in 1872 my paper was not well received. Indeed, many of my distinguished colleagues felt that the subject matter presented was obscene. However, after four years my experience has been enlarged and my views have become clearer and better defined concerning this whole matter.

The attempt to demonstrate the existence of what I call latent gonorrhea is surrounded by difficulties hard to overcome, to such a degree that I waited ten years after its discovery before I dared to put the matter into shape for publication. For, with all the advance in the physical sciences, I have been unable to bring forth a direct proof of its existence. In my work, published four years ago, I expressed the hope that the key to solve the question might be found in the presence of a fungus peculiar to the secretion of women affected with latent gonorrhea, to which my researches up to that time had given much encouragement. I have, however, not followed them up, for several reasons, principally owing to the fact that I found the same fungus in discharges from very young children, in cases where I was unable to trace all the points in the etiology of the case that would be necessary to establish the value attributable to the presence of this growth.

Another difficulty which is connected with the history of latent gonorrhea consists in the fact that the symptoms of the disease vary in almost every instance; and although it is possible to give a description of typical cases as I occasionally encounter them, they are met with rarely, one or another, or even the majority of signs not being present, or the disease so hidden by other uterine affections, more apparent to the senses, that its recognition is often a matter of difficulty and doubt. Furthermore, certain periuterine alterations, the result of latent gonorrhea, are so likely to escape detection by the most experienced of us, that a majority of the cases fail to receive as yet their true appreciation.

Again, our branch of the medical sciences being of recent development, the views entertained by its most eminent representatives as to the clinical importance of the several diseases of the uterus show a great discrepancy. It will be very difficult to convince followers of one or the other school that, in a case, for instance, of anteflexion and latent gonorrhea combined, the former is not the origin of all the disturbance in the functions of the organs affected, as well as of the system in general. I will now endeavor to give you a description of a typical case of latent gonorrhea.

Mr. M., a merchant of this city, formerly a commercial traveler for a large manufacturing firm in Europe, like almost every one of his tribe, acquires a gonorrhea. The treatment recommended by a renowned specialist is at once carefully followed, and the affection cured in two months.

Two years later this gentleman returns to Europe and marries a healthy, robust young lady from B., a village in the province of Westphalia, Germany.

Three months later, the woman begins to complain of backache and general malaise; it becomes difficult for her to attend to the common household affairs; the usual promenade, instead of being a pleasure, becomes fatiguing. Menstruation, which appeared hitherto without giving any preparatory notice, is now connected with backache, is more profuse than usual, and followed by a white discharge. By and by the desire to urinate becomes more frequent, and is occasionally accompanied by a sensation of burning at the meatus. The white discharge gradually extends from one period to the other. About eight weeks later a pain is felt in the left side of the abdomen, which suddenly increases upon an unusually severe exertion, to such an extent that the patient has to take to her bed. At the same time the dysuria is considerably increased, the discharge becomes profuse and of a greenish-yellow color, like matter. The physician attending her recognizes an acute attack of perimetritis. A year after this she consults me for sterility. I find her suffering from general weakness, backache, pain in the left side, increased before the now scanty menstruation, and a mucopurulent discharge. On examination, the uterus is found in right latero-version, and anteflected; the left vaginal roof, or parts above, hardened and contracted; the uterus soft, succulent, very tender on being gently pushed into its normal position; great tenderness of posterior cul-de-sac, neck of a high color, os surrounded by a thin rim of eroded tissue, discharging a tenacious yellow mucus; both outlets of Cowper's glands eroded to some distance, and painful to the touch.

Now, Mr. President, this combination and development of symptoms, physical as well as rational, you never will encounter in women who are married to husbands who have not exposed themselves to the danger of venereal affections, I say, advisedly, never. And if anyone has a right to speak thus positively, I claim this privilege.

In the history of this patient we find no trace of the existence of acute gonorrhea, either before or after marriage; but a condition very like, if not truly gonorrhea, is being developed during the acute attack of perimetritis.

You will now begin to understand why I have chosen the term "latent gonorrhea." The patient has never been infected in the accepted meaning of the word, but she gradually develops a condition which we usually observe as the result of an attack of acute gonorrhea And still the husband is apparently cured, not only according to his own opinion, but by that of his physician.

I have chosen the term latent gonorrhea instead of chronic gonorrhea, first, for the reason alleged above, that the patient is being gradually infected without any apparent symptoms of disease developing themselves in the beginning. I

have chosen this name better to define the truly imperceptible manner by which the disease works its slow progress in the organs affected up to the first more or less severe attack, when it passes from the latent into the active state; and second, because the disease in the female, although she be discharged, cured to all appearances, after an attack, say of gonorrheal ovaritis, keeps within her, at least up to the time of menopause, the germ of similar more or less severe relapses. The gonorrhea, after an acute attack, has simply returned to its state of latency to rest there, for months or years, the patient meanwhile being always in danger of a renewed outbreak, on proper provocation.

Admitting the persistence of gleet in the male after its outward disappearance, the question remains, how does it affect the female?

The course of the disease is only in comparatively few instances so well defined as in the case related above. We can, however, point out four different and clinically distinct groups of manifestations of the gradual infection of the woman by the repeated contact with minute quantities of the poison. It appears, first, as acute perimetritis, second, as recurrent perimetritis, third, as chronic perimetritis, fourth, as ovaritis.

All of these affections are accompanied by a catarrah of several sections of the mucous membrane. Often this catarrh is the only symptom present.

To sum up, let me state again by what means we may distinguish a catarrh of gonorrheal origin from a simple leucorrhea. It is of gonorrheal origin, if you find the following combination:

1. A red, eroded, narrow rim around the os.

2. Signs of existing or previous pelviperitonitis, such as tenderness of the parts above the roof of the vagina, contracted uterosacral or broad ligaments, lateroversion of the uterus, swollen and dislocated ovaries.

3. Catarrh of the whole or part of the vulva, the latter confined to the outlets of the vulvovaginal and periurethral glands; occasionally the presence of condylomatous excrescences of small size in the fourchette, or around the urethral orifice.

4. The absolute, or almost absolute, incurability of the discharge.

5. The fact that it began to develop in a healthy woman during and soon after a mere physiological change in the function of the sexual organs, namely, after marriage, without the intervention of any other recognized morbific cause.

If you find all, or the majority of these circumstances present, your diagnosis admits of no doubt.

I have taxed your patience, Mr. President, already too long, I am afraid, and therefore hurry on to the consideration of the last and most important question, that of the influence of latent gonorrhea upon fecundity in women.

It was this chapter of sterility in connection with latent gonorrhea which called forth the most—let me say—passionate criticism, here, as well as in Europe. This year I have to lay before you more statistics, which will not materially alter those published four years ago.

It is especially this class of patients suffering under the bane of sterility, which is met with in the consulting rooms of our prominent gynecologists; they are found to make the rounds among our specialists, applying to one after another for relief. Let us be candid, and confess that the reason why the statistics of our treatment of sterility are not coming forth is simply due to the scarcity of results obtained by our present means. And of all the several varieties of sterility, this one, except that caused by congenital malformation, resists treatment most obstinately. Long before the views represented in this paper had developed themselves in my mind to their present state of completeness and conviction, I was struck by the fact that, of two patients who came under treatment with apparently the same affection, say anteversion with catarrh and cervical erosion, who exhibited no difference either in their constitutions or external circumstances, one was rapidly cured, while the same remedies procured only temporary relief with the other. The former becomes pregnant after the cure of the ulceration, while the latter remains sterile. In the last class, you will find only one in fifty who is married to a husband who has not suffered from gonorrhea at one time or another of his life.

The presence of gonorrhea explains:

1. Why so many healthy, blooming, young girls, begin to suffer and fail as soon as they enter the bonds of marriage.

2. Why so many apparently healthy young women remain sterile.

3. Why the patient labor of our best physicians is so often thwarted in the attempt to cure certain affections of the female genital organs. It explains to some extent the prevalence of uterine diseases in large cities, and their increase during the last twenty-five years.

To conclude, I will sum up the result of these considerations in the following manner:

1. Gonorrhea in the male, as well as in the female, persists for life in certain sections of the organs of generation, notwithstanding its apparent cure in a great many instances.

2. There is a form of gonorrhea which may be called latent gonorrhea, in the male, as well as in the female.

3. Latent gonorrhea in the male, as well as in the female, may infect a healthy person either with acute gonorrhea or gleet.

4. Latent gonorrhea in the female, either the consequence of an acute gonorrheal invasion or not, if it pass from the latent into the apparent condition, manifests itself as acute, chronic, recurrent perimetritis, or ovaritis, or as catarrh of certain sections of the genital organs.

5. Latent gonorrhea, in becoming apparent in the male, does so by attacks of gleet or epididymitis.

6. About 90 per cent of sterile women are married to husbands who have suffered from gonorrhea either previous to, or during, married life.

Discussion of Paper of Dr. Emil Noeggerath by Dr. J. Marion Sims*

The paper to which we have just listened is full of interesting and provocative observations put together by a gynecologist whose training in the German clinics is reflected in his thorough and meticulous study of this subject. His views are not altogether new to some of us, as the author has already published a paper on the same subject in one of the German medical periodicals. Incidentally, his views met with violent opposition from his German colleagues, just as I believe will be the reaction from the Fellows of this newly organized Society of the leaders of American gynecology.

If Dr. Noeggerath's conclusions are correct, thousands of young men stand convicted of inflicting chronic invalidism and often death on the brides whom they have sworn to cherish and protect, and thousands have robbed their wives as well as themselves of the happiness of parenthood. This is a grave indictment, and one which cannot be accepted without challenge.

With characteristic Teutonic thoroughness, the essayist has marshaled an imposing array of observations and has erected a mountain of evidence, but upon a foundation of sand. In at least some of the numerous cases analyzed by Dr. Noeggerath it must be admitted that a possible relation with the latent gonorrhea of the husband cannot be ruled out. In the largest number, however, far more logical explanations suggest themselves for the wife's perimetritis, recurrent perimetritis, chronic perimetritis or ovaritis, these being the diseases enumerated by Dr. Noeggerath as due to gonorrheal contamination by the husband.

To give but one of many examples, he includes in his recital a case in the treatment of which I was concerned. The patient's problem was that of sterility, for which I recommended and carried out incision of the cervix, a procedure which I have found frequently effective, and which I described in my recent monograph on sterility. The acute perimetritis which followed the cervical incision was the result of the operation, this being one of the hazards to which I called attention in my monograph. And yet Dr. Noeggerath ascribes it to the gonorrhea which the patient's husband had contracted one year before marriage. This form of *post hoc propter hoc* reasoning illustrates the fallacies revealed in many of Dr. Noeggerath's case reports.

He emphasizes the infecundity of women whose husbands have had premarital gleet, but he ignores the far more numerous instances of sterility in women whose husbands had never been afflicted with this loathsome disease. Nor does he seem to recognize the fact that many men known to have had gonorrhea before marriage have been fathers of large families of children.

One of the Fellows of this Society, present here today, Dr. Joseph Taber Johnson, permits me to cite the results of a study which he recently made of the marital histories of twenty medical colleagues who acknowledged having had gonorrhea before marriage. In not a single case did the wife suffer any of the horrendous results pictured by Dr. Noeggerath, and every one of these marriages was blessed with a large family of children.

I confess I did not relish the disparaging comment made by the essayist concerning the method of testing the fertilizing potency of the semen which I have described, and which is being spoken of as the Sims test, especially in England, where I first publicized the test. It is based on the presence and the viability of spermatozoa recovered from the cervical canal rather than from the vagina. I venture to predict that this test will live far longer in gynecologic practice than will the concepts of Noeggerath.

In his paper the author speculates upon a fungus of some sort as the cause of gonorrhea. His opinions would carry far more conviction if he could show us such an organism under the microscope. Perhaps he will carry his speculation farther, and hold out for us the hope that some day he will discover for us another fungus or mold capable of destroying the mythical fungus of gonorrhea.

One can imagine the consternation and the social chaos which would result if the views which we have heard today became public property, and if they were stamped with the im-

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primatur of such an organization as we have created at this meeting, an organization which we confidently hope will assume leadership in all questions pertaining to the special health problems of the women of our country. The sacred institution of marriage would be imperiled by the shocked surprise, indignation, resentment, and suspicion engendered in the minds of our people, and especially of our women. One can imagine a day when a man's proffer of marriage would not be acceptable unless it were accompanied by a sworn affidavit of premarital chastity or a medical certificate of freedom from premarital venereal disease. It is not a pleasing prospect, and hence I have been moved to express the disapproval which I believe is shared by all the Fellows here present of the unsavory and unjustified conclusions set before us by the author of this paper.

PRESIDENTIAL ADDRESS*
Adventure at Avernus

FREDERICK C. IRVING, M.D., BROOKLINE, MASS.

IN THE latter part of the last century there is said to have lived in Boston an obstetrician and gynecologist whose name was Endymion Jones. The son of a professor of classical literature in a small New England college and named for the beautiful youth beloved by Selene, the moon goddess, it was natural that among his earliest ventures into literature he formed an acquaintance with the works of Virgil, Ovid, and Homer, as well as with Bulfinch's *The Age of Fable*. In his mature years, therefore, although in active practice and keenly aware of contemporary events in medicine and in the world at large, the background of his childhood often led his thoughts into the fairy realm of mythology. The persons and events of those legendary days possessed for him a reality that was missed by others of his time who could view them only through the mist of antiquity. To Jones, the Milky Way was no mere galaxy of stars that adorned the heavens but the actual pathway of the gods that led them to Olympus; he knew also that there must be naiads on the slopes of the neighboring Middlesex hills, lovely river nymphs, their hair entwined with rushes, each pouring from her marble vase the waters which formed the several sources of the Charles.

Endymion Jones is important to us because in 1876, the year of our birth as a society, he traveled in Italy and described in his journal a certain amazing adventure in the vicinity of Naples. This manuscript is even more extraordinary, for not only does it provide us with a glimpse of some national and world events as well as of the obstetrics and gynecology of his time but, thanks to his encounter with a famous seeress, it also assumes the nature of a prophecy. In fact, so accurate are the predictions embodied therein that certain skeptical persons might even question its authenticity. But let us, without further preface, open the journal of Endymion Jones and hear what he has to say.

* * *

Late in the fall of 1876 (he writes) while spending a few days in Naples, the idea possessed me to visit the Lake of Avernus. You will recall that Aeneas while seeking the spirit of his father, Anchises, met the Cumaean Sibyl in a cave on its shore and descended with her into the nether regions. Early one morning, therefore, I embarked in an omnibus and set out for the little village of Baiae, which lies some 15 miles due west of the city. A short walk from where I was put down brought me to the shore of the lake which, contrary to the forbidding description in the Sixth Book of the Aeneid, I found to be of

unusual beauty, bordered by hills covered with olive groves, chestnut trees, and vineyards, and reflecting from its calm surface the brilliant blue of the Campanian sky. I set about exploring the many grottoes and caves on its southern shore, and as I approached the largest of these caverns my feet dislodged some fragments of solidified lava with which the ground was covered, sending them into its entrance with a resounding noise. To my astonishment I heard a voice from within which addressed me thus:

"Approach, mortal, for such you must be since no spirit could create such a clatter."

Startled by the voice, for I had seen no one since my arrival at the lake, I peered into the cave and beheld a very old woman standing in its entrance. She was erect in stature and of commanding presence. A robe enveloped her entire figure; its upper portion was drawn over her head in the fashion of a hood and beneath it I saw a face furrowed by the years, but which in youth must have been surpassingly beautiful. Her brilliant eyes viewed me with speculation.

"I am the Sibyl of Cumae," she said, "and who are you?"

I told her my name and the city in which I lived, informed her that I was a physician specializing in midwifery and the diseases of women, and explained my presence by my interest in classical antiquity.

"Antiquity indeed," she replied somewhat tartly. "You can see that although I am no longer young I am just as much alive as I ever was. But I have no wish to appear ill-natured. As you know, I meet here the spirits of the dead, who must await their turn to enter the realm of the departed and be judged according to the balance between the good and evil in their lives. Those whose errors have been grievous are forthwith consigned to Hades. On the other hand, those whose earthly spans have been useful and whose sins have been only little ones pass on to the delights of the Elysian fields. I am happy to inform you that there is a large number of doctors there, but it would surprise you to learn how many lawyers have not been so fortunate. Most shades I meet are too apprehensive about their fate to tell me much of what is going on in the outside world; but perhaps you, not yet ready for the afterlife, would be willing to relate some of the important events that have taken place this year among the living."

"It would give me great pleasure," I replied. "In my country President Grant is nearing the end of his second and last term. There has been much corruption in Washington, but the old General has been unaware of it, and although he was not a good president history will say of him that as a soldier he served the country well."

"Jones," said the Sibyl impressively, "the days of presidents who do things for your country have about passed. Some years from now presidents who do things to your country will appear, and the most notable event of this nature will occur on March 4, 1933—I can give you the exact date. Beginning then your national capital will swarm with curious characters: immature theorists who will have as laboratory subjects almost 150 million people upon whom they will be free to try their impractical ideas. There will come a time when Don

Quixote, Ophelia, and the Mad Hatter could circulate freely in Washington official life and not be thought in any way peculiar.''

"Many things lie in the future which I should like to tell you,'' she continued, "for you seem to be an intelligent young man, but let us sit before the cave in the cool of the shade while I first explain my gift of prophecy; or, if you have heard the story before, allow me to refresh your memory. I am no goddess but a mortal like yourself, born with the ability to tell the future and once beloved by Apollo. One day when we were walking on the beach not far from here, to win my favor he bade me fill my hands with sand, and he promised that I should live a year for every grain of it that I could hold. When he became more ardent in his wooing and his actions assumed an unmistakable design, I repulsed him, for I was young and inexperienced. He departed in a rage; and while he kept his word about long life, he assumed a revengeful attitude and allowed me to grow old like other people. As it is I have lived far beyond the human span, but my vision of the future is becoming dim; I can see ahead clearly only for three-quarters of a century—after that everything is dark.''

She sighed. "I wish now that I had been less coy.''

"You Americans,'' she continued, "so far have been a fortunate people. Your government, founded on the political philosophy of John Locke, who you will recall was a doctor, has abolished the divine right of kings, assured the consent of the governed and the rule of the majority and has, moreover, provided that neither the executive nor the legislative branch shall be supreme. Your nation was the first to enjoy these benefits and already she has possessed them for a hundred years, but I am fearful of the future. There is now living in London at the age of 58 an exiled German named Karl Marx who with Friedrich Engels published 29 years ago a document entitled *The Communist Manifesto*. In it they advocated that all property in land be abolished, that the rights of inheritance be eliminated, that the possessions of emigrants and rebels be confiscated, and that labor be made compulsory. As milder measures they favored a progressive income tax, the nationalization of transportation and communication, and the entry of the State into what has always been considered private enterprise. I can tell you now, Jones, that 75 years hence your country will have had an income tax for well over two decades, an inheritance levy of almost confiscatory size, and not only will the government be competing with many private industries but it will also have adopted a heckling policy toward many others. The income tax will appear because your inefficient government will be unable to function without it. As justification for the expropriation of a large portion of all estates it will be said that since the heirs did not accumulate the property they are not entitled to it and so it should go to the government. Neither, for that matter did the government accumulate the property. Both taxes have their origin in communism; you can read about them in *The Communist Manifesto* and *Das Kapital*. Other Marxian doctrines will creep into your democracy, some by a stealthy process of concealed osmosis and others under the guise of great social benefits conferred upon the faithful by a beneficent government. In a watered-down form and under the name of

socialism, which looks to me like communism minus the mass executions and the salt mines, the Marxian ideology will be espoused by as sensible a nation as Great Britain; in that country even medicine will be socialized and most doctors will work for the government.''

''What will be the result?'' I asked.

''I cannot see the ultimate outcome,'' she replied, ''but the first year this scheme is in operation there will be over 72,000 more deaths. It is obvious that socialized medicine is not likely to save a greater number of lives.''

''Shall we have it in the United States?''

''Seventy-five years from now,'' she replied, ''under the misrepresentation of free medicine for all, it will be another bait dangled before the voters by the politicians, like the 'bread and circuses' of which Juvenal spoke as long ago as the first century of the Christian Era. The art of befuddling the populace has not changed much in eighteen hundred years; in fact Plato, who died 347 years before the birth of Christ, said that lying is the prerogative of the government just as medicine is the prerogative of the physician. However, for a time at least, a wasteful administration will have spent so much money that the country will be unable to afford it.

''But to return to the communist story. Let me tell you about a person named Lenin, who is now only a lad of six years. What I have outlined already is but small beer to the heady draught that this individual will offer. He will preach the use of terror, the disregard of all human and personal rights, and the destruction of every standard of veracity and ethics. Russia, that sprawling giant, will set out to conquer the earth and impose by force her ideology on all mankind. Her aim will be to erase every spiritual value which human beings have acquired since they left their caves and emerged from their forests and to reduce their morality to that of savages. At no time since the beginning of history will civilization face so great a danger.

''But enough of political philosophy. What of importance is going on in the world in 1876?''

''During this year Bell has invented the telephone. It is a device which transmits the voice over a wire.''

''I can see,'' said the Sibyl, ''that it may be a boon to patients, but on occasions it will prove a curse to doctors, especially at dinner time or in the early hours of the morning. What else?''

''The first internal combustion engine has been built, and it may have far-reaching consequences. Two other notable events in America have taken place in 1876: the founding of Johns Hopkins University and the establishment of the National Baseball League.''

''I would say,'' remarked the Sibyl, ''that you have mentioned them in the direct order of their scientific importance but in inverse ratio to their popular interest.''

''I hope,'' I continued, ''that you will not think me too complacent with the times when I say that these are particularly fruitful days in literature and the arts. Although the great writers of New England have now passed their zenith, in Great Britain, Tennyson, Browning, and Cardinal Newman are alive,

as among the scientists are Darwin and Huxley. Present French authors are de Maupassant, Loti, and Flaubert, and the current great painters in that country are Monet, Renoir, and Cézanne. This year also I heard at Bayreuth the Ring when it was performed for the first time in its entirety."

"On the whole," said the Sibyl reflectively, "I think you are living in a fortunate time in the world's history. Aside from a Russo-Turkish war ending in 1878 there will be peace in Europe for 38 years. But I am curious about the current state of your specialties, obstetrics and gynecology. You can speak to me almost as one physician to another, for during my association with Apollo —he is, you know, the medical attendant to the gods—I acquired an extensive professional vocabulary, and you know how much doctors like to talk about their work. Tell me, to begin, how dangerous is it to have a baby in this last quarter of the nineteenth century?"

"Fortunately, I have the facts at hand," I replied, "and you may judge for yourself. Playfair, the English obstetrician, has just published a textbook in which he reports that one woman in every 130 delivered in his country dies within two weeks. Numbers are not available for the entire United States, but in Massachusetts the death rate is one in 173. At the Rotunda Hospital in Dublin one patient in every 50 has died this year."

"I shall amaze you," said the Sibyl, "by predicting that 75 years from now less than one mother in every 1,000 delivered in your country will lose her life, and in your State only one in 1,400. As for the baby, his chances of survival will be twice as good. This astonishing improvement, one of the greatest triumphs in the history of medicine, will be achieved by the doctors themselves and no socialistic governmental scheme will have had any part in it. But why are things so bad at the present time?"

"The chief causes of maternal deaths have always been childbed fever, hemorrhage, and puerperal convulsions," I answered, "and of these childbed fever kills the greatest number. During a recent epidemic affecting a hospital in one of our largest cities one woman died in every 5 delivered."

"But surely you doctors know that this disease is passed from one patient to another," she said, "Your fellow townsman, Holmes, as well as the Hungarian, Semmelweis, told you that almost 30 years ago. Moreover, Lister, the British surgeon, has been using a method for the past nine years which has greatly reduced infection in his operations and Bischoff of Basle has applied it to obstetrics. It seems to me that you *accoucheurs* have been asleep."

"We still do not know the actual cause of the infection and we find it difficult to attack an enemy we cannot recognize," I replied apologetically.

"Two years from now," she said, "Koch will demonstrate that harmful bacteria exist not only in infected wounds but also on the healthy skin itself, and in the following year Pasteur will prove that the streptococcus is the chief cause of puerperal fever. In six years von Bergmann will introduce the aseptic technique, whereby bacteria will be eliminated at surgical operations and at childbirth by the sterilization of instruments and dressings, prolonged scrubbing of the operator's hands and the patient's skin, and the use of antiseptics. A new era in surgery and obstetrics is in the making. In the second and fourth

decades of the next century two groups of drugs, the sulfonamides and the antibiotics, will to all intents put an end to childbed fever, and the fear that now haunts the lying-in chamber will be gone forever.''

"What proportion of deaths follow that spectacular operation, cesarean section?" she continued.

"About three in every five. My friend, Harris, tells me he finds that a woman in labor stands a better chance of survival if she opens her own abdomen in desperation or is gored by an infuriated bull than if she is operated on by the experts in New York City.''

"It would seem to me as a mere female and hence somewhat of a seamstress," said the Sibyl, "that if I had cut the uterus open to take the baby out I would think it neater to sew it up, but it will be six years before Sänger will introduce this method to the medical profession. This obvious measure, joined with von Bergmann's aseptic technique, will bring about a vast improvement. In 75 years not more than one mother in 200 who has this operation will be lost; in fact its danger will be diminished to the point that it will be performed many times when there will be no need for it.''

"What do you know about the cause of puerperal convulsions?" she inquired.

"The best opinion of the present day ascribes them to a special form of Bright's disease that affects only pregnant women.''

"That is an erroneous belief," she replied, "but you will be surprised to learn that 75 years from now the doctors still will not know what causes it, although they will have a much clearer idea of how it works its ill effects in the body.''

"One in every three or four eclamptics die," I resumed, "but I am afraid that the methods used to save them, such as *accouchement forcé*, purging, and bloodletting, only hasten the end.''

"I have no doubt of that," she said, "but when doctors learn to examine their patients frequently during pregnancy, an event which will come only with the turn of the next century, they will be able in most instances to prevent the disease, and when it does occur a more conservative therapy will reduce the mortality to about 2 per cent.''

"As regards hemorrhage, the other chief cause of maternal death," I continued, "we lose about one-quarter of the women with placenta previa; and concerning internal concealed bleeding from premature separation of the placenta, a study just completed by Goodell shows that one-half of the mothers and almost all the babies succumb.''

"Here again," said the Sibyl, "the future holds great promise. I predict that deaths from placenta previa will fall to about one twenty-fifth of what they are and those from concealed hemorrhage to about one-seventeenth. Great benefit will follow the safe and free transfusion of blood. I understand that even today transfusions are occasionally performed.''

"A medical writer has recently reported 243 transfusions prior to 1873," I replied, "and one-third of them have failed, but the use of the lower animals,

sheep, for example, has been abandoned, because each time the recipient died.
I understand, also, that they lost a certain number of sheep.''

"What recent improvements have been made in the treatment of extra-
uterine pregnancy?''

"None," I replied, "for so far all operations have been in cases where the
fetus has become encapsulated and died, and no interventions have been under-
taken at the time of rupture.''

"Seven years from now," said the Sibyl, "Lawson Tait, an ill-mannered
but able Scot, will be the first to establish the surgical treatment of this con-
dition, but it will not be until 1891 that Schauta will prove conclusively that
prompt operation will increase the chance of survival fifteen times.''

"Now let us turn to the sister specialty, gynecology," she continued.

"As a matter of fact," I replied, "gynecology is just coming into being, for
in recent years more significant advances have been made than have occurred
in the entire history of the specialty. Until a short time ago the treatment of
the diseases of women was a sorry affair. It consisted mostly in poking pessaries
and packs into place and in painting the cervix. Living in this Victorian age
when womanly modesty is a belligerent virtue, progress has been retarded by a
definite taboo. Charles D. Meigs, that consistent obstructionist, who immortal-
ized himself by denying the infectiousness of puerperal fever and by opposing
anesthesia in childbirth, has objected to pelvic examinations as likely to induce
a lax moral sense in the ladies of Pennsylvania's largest city. His later fellow
townsman and my contemporary, Goodell, now says that such investigations are
permissible if the doctor the while keeps his eyes fixed on the ceiling. Let us
hope that in the fairly brief interval which has elapsed between these two gentle-
men the virtue of fair Philadelphians has undergone no serious deterioration.''

"In spite of these handicaps," I continued, "I foresee a bright future for
gynecology, for there is an increasing group of daring individuals who do not
hesitate to resort to surgical procedures. It is now 67 years since Ephraim
McDowell made history by his operation on the woman who, encumbered by
her huge ovarian cyst, rode over the mountains to the little village of Danville,
Kentucky. Great as was his courage in embarking on an undertaking that had
never been achieved, it pales before her fortitude and faith. Fortitude she had
in the highest degree; as for her faith, who can say whether it arose from con-
fidence in her doctor or from ignorance of the presumptive fatal outcome. In
medicine, as sometimes in religion, the line between faith and ignorance is not
too finely drawn. But even so, Jane Crawford is one of the neglected heroines
of medicine. James M. Venable, upon whom Long operated under ether in
1842, and Gilbert Abbott, the subject of Morton's demonstration in the dome of
the Massachusetts General Hospital four years later, were heroes, too, for so
far as either knew there was a distinct chance that he might not wake up. I
hope that some day the world will place the bravery of the patient above the
boldness of the surgeon, for there is where it belongs.''

"Since McDowell," I went on, "many ovariotomies have been performed.
In America at present the two Atlees are pre-eminent; they have operated over
400 times and not too many of their patients have died. But without doubt

the leading ovariotomist in the world is Spencer Wells of London; his death rate is only 1 in 25, and he has accomplished this by the exercise of scrupulous cleanliness as applied to his instruments, his hands, his sponges and dressings as well as to the skin of his patients."

"And this before Lister, Koch, and von Bergmann," added the Sibyl.

"It seems to me, however," I continued, "that the gynecologists of my day assume a most unfriendly attitude toward the ovaries. They are removing them for dysmenorrea, menorrhagia, amenorrhea, ovarian neuralgia, whatever that may be, and in fact for what appears to be no reason at all. Moreover, because of the dread of peritonitis in abdominal operations they are abstracting them through the vagina in an underhand and furtive fashion."

"In the middle of the next century," said the Sibyl, "certain practitioners of your specialty will exhibit the same animosity toward the uterus. Hysterectomy will have become so safe that almost anyone can and will perform it. Things will arrive at such a pass that a woman who completes the menopause with her uterus *in situ* will not only have possessed an unusual degree of elusiveness, but she will also be an object of curiosity among her friends."

"At the present time," I resumed, "hysterectomy is a perilous venture and he is a bold operator who attempts it, for here we are concerned not only with the danger of peritonitis but also with the risk of death from secondary hemorrhage by slipping of the ligature tied about what is left of the uterus after the tumor is removed. In fact so often fatal is the operation that my friend Byford recommends instead the use of ergot to cause sloughing of fibroid tumors in the hope that they may be passed by vagina."

"The first man to overcome the risk of hysterectomy," said the Sibyl "will not be a gynecologist at all but a general surgeon, Stimson of New York, who in 1889 will be the first to ligate the ovarian and uterine arteries before removing the uterus, and by this obvious detail in technique he will add more to the safety of the operation than all the specialists in diseases of women up to that point."

"As for cancer of the uterus," I continued, "there is still little to add to the statement made by Churchill in 1850 when he said: 'This is the most fearful and uniformly fatal disease to which the uterus is obnoxious; it is the most irresistible in its progress and the least amenable to treatment.' So far no one has removed the uterus for cancer."

"Two years from now," replied the Sibyl, "hysterectomy for cancer will be performed for the first time by Freund of Breslau who will employ the antiseptic technique of Lister, but in 1900 Wertheim of Vienna will introduce the operation which will bear his name. Five years later Abbe of New York will begin the use of radium, and in 1913 at the Congress of the German Gynecological Society it will be reported that 35 per cent of the patients treated in this way will show no recurrence of the disease after 5 years. Much later, in the 1940's, a much more extensive operation than that of Wertheim will be performed on patients who hitherto will have been considered beyond surgical intervention with some success in the prolongation of life."

"The most outstanding achievement in contemporary gynecology," I resumed, "is in the field of plastic surgery, which Sims and Emmet have developed to a high degree. Because of his cure of vesicovaginal fistula and also by reason of his vivid personality, Sims has won international fame, but operations performed by Emmet are more varied in character."

"As a matter of fact," said the Sibyl, "procedures based on those of Emmet will be standard 75 years from now. I would say that while gynecology is one of the greatest adoptive mothers in medicine, for she acquires anesthesia and the technique of hysterectomy from general surgery and asepsis from both surgery and bacteriology, the plastic operation is the child of her own conception."

"Now," she continued, "let me tell you about certain important discoveries that will be made early in the twentieth century. These concern the internal secretions of the ductless glands which have to do with sex. I shall not describe them to you thoroughly for it might confuse you; indeed some gynecologists and obstetricians 75 years from now will be none too clear on the subject. But one of them is the female sex hormone; it makes a woman a female and it will be found also in the lower animals and even in plants; there will be traces of it in such an outlandish place as the water of the Dead Sea, although what it will be doing there baffles my imagination. By the same token it will be discovered that there is a male sex hormone that makes a man a male. But time does not permit me to speak further of these extraordinary substances; let me rather in the short period that remains deal briefly with two peculiar notions which will engage the attention of obstetricians three-quarters of a century from now. One of these will be called 'natural childbirth.' In brief this means childbirth without anesthesia. The Palaeolithic mother delivered her baby by 'natural childbirth' but this fact will not justify Palaeolithic methods in the middle of the twentieth century. When Simpson died six years ago a day of public mourning was decreed in his home city and 30,000 people attended his funeral. It would indeed be difficult to convince the women of Edinburgh, or, for that matter, the women of the civilized world, that he had made a mistake when he introduced anesthesia to relieve the pains of labor. The advocates of 'natural childbirth' will say that if a woman is given no anesthetic she will have a more secure sense of motherhood and a greater love for her baby. If by a more secure sense of motherhood they mean that she will be sure she has had a baby, certainly they will be right about that. As regards the other alleged advantage, if I knew that I could give birth to an infant without suffering and deliberately elected to endure the pain which accompanies that act, I should doubt my own intelligence; and so far as my feelings toward the baby are concerned, I fear that I might actually dislike the brat."

"There will also appear at this time," she continued, "a group of self-constituted authorities who will be known as child psychologists. They will maintain that a newborn baby should not be fed at regular intervals but only when he cries; otherwise, they say, he will be frustrated and will grow up with a sense of inadequacy. How they know this they will not tell us, nor will they inform us regarding any personal interviews they have had with nurslings. My

own opinion, and like all spinsters I have definite ideas on the rearing of children, is that the young need more discipline rather than less, and that this is a wise precaution to prevent them from growing up into little monsters. But the natural common sense of the laity may be counted on eventually to dispel these notions, both of which impress me as a trifle silly.''

"The science and art of pediatrics will also have made great advances in 75 years," she resumed, "but it seems to me that the practitioners of that specialty will miss the greatest discovery of all time; a discovery which would be of tremendous hygienic and social importance and would insure the immediate canonization of the man who made it by all mothers of young children. That discovery, Jones, would be a means of abolishing the diaper. As I look into the future I see that in the year 1951 there will be one billion diapers used in the United States alone. I am naturally good at arithmetic, and to indicate the vast magnitude of the problem I shall give you the results of my calculations, which are these: Placed end on end these diapers would reach to the moon and back, those remaining would encircle the earth at the equator 11 times, and there would be enough left over to extend from Boston to Alaska. But, alas, I fear that this millenium will never affect the nursery."

"And now," she continued, "it is time for me to go. While we have been talking a considerable number of shades, awaiting their turn to enter the nether regions, have gathered about us, although you cannot see them. I hope that they have been edified by our conversation, and I hope also that you have not thought me a garrulous old woman."

"By no means," I replied. "Every moment of our visit has been a pleasure to me. For my part, I have always found elderly women delightful. Once past the climacteric, the natural predatory instinct of the human female disappears, for the hunt is over. It is no longer so vital to make a good impression and her natural charm shines forth untrammelled."

"I trust that you will not forget me," she said. "There is a portrait of me in the Sistine Chapel; it is by Michelangelo, who had never seen me, and it is most unflattering, for it depicts me with the face of an Indian warrior and the body of a wrestler. When he passed through here in 1554 I called his attention to this *faux pas*, and you may be sure that it did him no good."

"I shall need no portrait to remember you by," I said.

She smiled. "I have enjoyed our conversation, too."

As the Sibyl ceased to speak there was a sudden darkness accompanied by a violent burst of rain, so that the opposite shore of the lake was hidden and its surface, so placid before, was whipped by the wind into small but angry waves. A brief squall, sweeping down the valleys of the Apennines, as is frequently the case in this part of Italy, was upon us before we were aware of its approach. In a few minutes it was over and the sun was shining again. I looked for the Sibyl, but she had disappeared; I called to her, but there was no reply.

*   *   *

So ends the story of Endymion Jones. There are those who say that no such person ever lived, that his name is missing from the contemporary city

directory of Boston and the register of the Massachusetts Medical Society; nor is his tombstone to be found in the Old Granary Burying Ground or in Mount Auburn Cemetery. On the other hand how could a man who never lived have written a journal; and how, unless he had encountered the Sibyl at Avernus, could he have predicted with such certainty the extraordinary changes that have taken place in the world at large and in our specialties? But if he really lived and died, let us think of him now not as a dweller in some prim New England heaven, consorting with university presidents, deans of medical schools, trustees of hospitals, and other dull people, but as relaxing in the eternal sunshine of the Elysian Fields, seated on a flowery bank beneath a laurel tree and engaged in happy conversation with his friend, the Cumaean Sibyl, who by this time must be indeed a very old lady.

ENTEROCELE*

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ANATOMICALLY, the cul-de-sac is that portion of the pelvic peritoneal cavity which extends below the level of the uterosacral ligaments. Gwillim regards the pouch of Douglas as being like a basin supported in a wicker basket. "The uterosacral ligaments represent the supporting basket. They extend from the second and third pieces of the sacrum to the postero-lateral aspects of the supra-vaginal cervix and the vaginal wall, as far down as the point of approximation of the vaginal fascia to the fascia propria of the rectum. It is at this point in the midline that the pouch of Douglas is weakest, since the caudal extensions of the utero-sacral ligaments do not quite come together, and the rectal and vaginal fasciae remain separate."

Bonney has shown that the uterosacral ligaments are not ligaments in the usually accepted sense, but are continuous with the cardinal ligaments of the vagina. He goes further and regards these as the posterior edge of the fan-shaped cardinal ligaments, spread out and twisted backward. Those who regularly perform radical abdominal hysterectomy of the Wertheim type for cancer of the cervix will appreciate, on inserting the hand between rectum and vagina in the course of this operation, that the dense cardinal ligaments of the vagina, when traced upward to their posterior edge, are confluent with the uterosacral ligaments on either side.

Bonney further regards the pouch of Douglas as a natural hernia with a sac, the cul-de-sac, and a neck of the sac, or hernial orifice, represented by the so-called uterosacral ligaments. The first important contribution to our knowledge of the anatomy of this area emanated from Denonvilliers, who in 1836 described the fascia which bears his name. Fifty years later, in 1899, Cuneo and Veau published their monumental work on the cul-de-sac and the rectogenital "space" and proved that the rectogenital septum was composed of fused dorsal and ventral peritoneum. In 1922 Wesson suggested that the rectogenital septum was purely fascial in structure, and in 1940 Curtis, Anson, and Beaton concluded that the interval between the rectum and vagina was occupied by "loose cellular tissue" with the vaginal fascia in front, and the rectal fascia behind. Recent work, however, by Kirk (1947) in England, and Uhlenhuth, Wolfe, Smith, and Middleton (1948), in this country, have to my mind confirmed the accuracy of Cuneo and Veau's original work and conclusions.

Kirk, as a result of his anatomical investigations, found that, initially, in the fetus, the urorectal septum is composed of solid mesoderm which later becomes excavated by an extension into it of the celomic peritoneal cavity. He states that at birth the pouch often extends to the level of the perineal body,

but that, later, it is obliterated by fusion of the peritoneal walls of the sac, and of course this fusion process may vary somewhat in its extent in different individuals.

In 1948 Uhlenhuth and his co-workers published in *Surgery, Gynecology and Obstetrics* the results of their researches into the embryology, anatomy, and variations in the pouch of Douglas. This research being of an anatomical nature has not attracted the attention it deserves from gynecologists. The results are based on conclusions arrived at after a series of most beautiful and meticulous dissections of adults, infants, and fetuses. They demonstrate that in fetal life, in many instances, the peritoneal pouch extends down to the level of the perineal body, but as the fetus nears term there is a gradual fusion of the dorsoventral walls of the pouch, and this fusion begins at the caudal extremity. This process of fusion varies in different individuals, and all gradations, from complete nonfusion to the normal, are encountered, and this of course explains the variability of the depth of the cul-de-sac. These workers have demonstrated that pressure on the floor of the cul-de-sac of the infant can reopen this fusion, and have shown in the adult that the rectogenital septum is nothing other than this fused peritoneal process. They show that the uppermost limit of fusion is often visible as a transversely puckered scar at the lower limit of the pouch, and they demonstrate that the septum fuses with the dorsal vaginal fascia, to which it is fairly densely adherent, while it is only lightly attached to the prerectal fascia behind. In the usual surgical approach to the rectovaginal space this peritoneal septum is invariably attached to the vagina, and appears on the ventral aspect of the space as a membrane of duck-egg greenish-blue color. Anyone interested can confirm in large measure the work of Uhlenhuth and his colleagues by noting the variability of the depth of the cul-de-sac in stillborn infants at term, and in premature stillborn fetuses, and by noting the ease with which the peritoneal process can be "unfused" by pressure on the pouch from above.

Through the courtesy and kindness of Dr. Uhlenhuth and the editors of *Surgery, Gynecology and Obstetrics,* I would like to show some illustrations demonstrating these researches.

The application of these anatomical findings to the clinical problem of, so-called, hernia of the pouch of Douglas is interesting in that these afford an explanation of the various types of enterocele encountered and indicate a rational means of surgical cure of the condition.

From the researches of Cuneo and Veau, Kirk, and Uhlenhuth and his workers, it would appear that a congenital elongated sac is frequently present from birth, and the analogy to the preformed sac of hernias generally becomes obvious. This so-called congenitally elongated sac may or may not produce symptoms, depending on whether or not the sac becomes distended with coils of intestine. This in turn is dependent on the length of the mesentery and its tone. One, frequently, in the course of pelvic abdominal operations, encounters an abnormally deep cul-de-sac which is completely symptomless, for the reason that the sac is not filled. In a few cases, however, especially in association with generalized enteroptosis or adiposity, distressing symptoms of down pressure on standing are evident, even in the absence of uterovaginal descent. This pressure may be accentuated in asthenic patients by a previous ventrofixation operation, which results in the inclined plane formed by the posterior wall of the ventrofixed uterus concentrating the thrust of the ptosed intestine to the
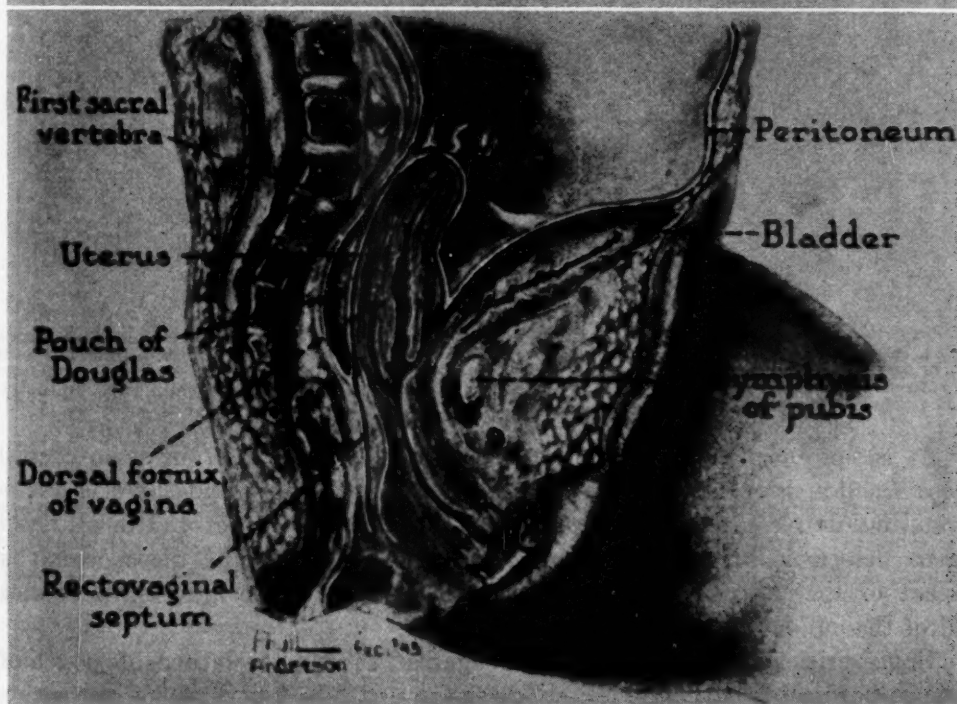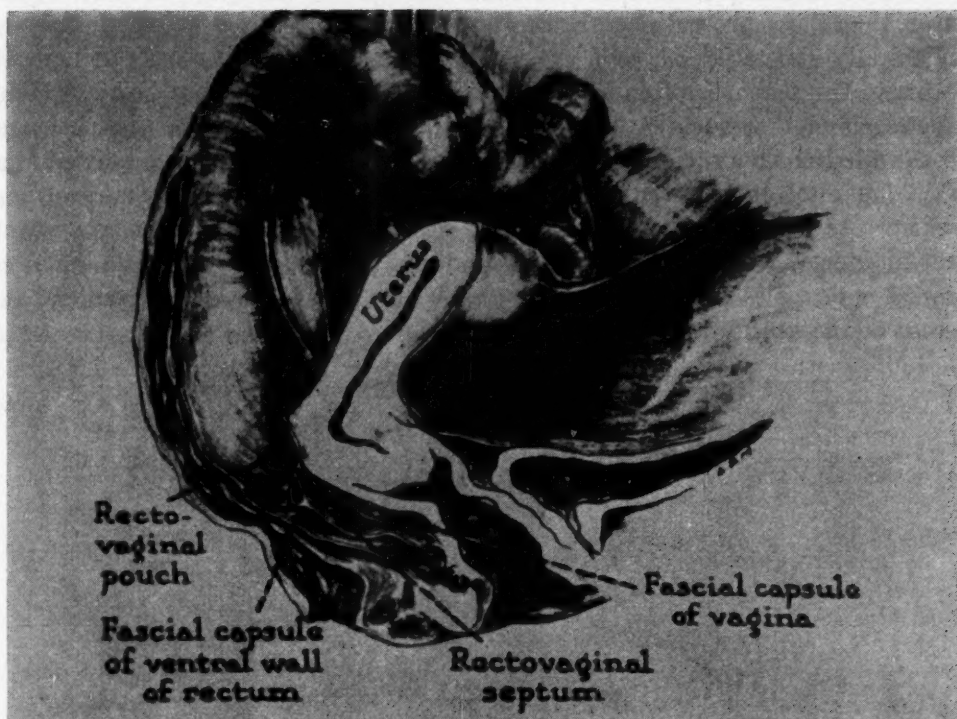
Fig. 1.

Fig. 2.

Figs. 1 and 2.—Drawings of dissections on two adult women showing clearly the fused dorsoventral peritoneum forming the rectovaginal septum. (From Uhlenhuth, E., Wolfe, W. M., Smith, E. M., and Middleton, E. B.: Surg., Gynec. & Obst. 76: 148, 1948.)

apex of the cul-de-sac. I have chosen to call these *pulsion* enteroceles for the reason that these protrusions are the result of pressure from above on either a congenitally elongated sac, or a sac which becomes elongated purely as a result of thrust from above, often in association with some weakness below. Many workers claim that such a thrust is the important factor in the production of the so-called congenital or virginal prolapse, though it must be admitted that some congenital or acquired weakness of the lower supporting mechanism must co-exist. As opposed to pulsion hernias, enteroceles are a frequent accompaniment of uterovaginal or rectal prolapse, and to these I have given the name of *traction* enteroceles for the reason that such hernias are the direct result of the descent of the uterus and vagina.

Fig. 3.—Pelvis of a Negro infant born at term, seen in the dorsal view after removal of the sacrum, coccyx, and rectum. The dorsal wall of the vagina is incised longitudinally and is seen to be covered in its entire length by peritoneum. The rectovaginal pouch extended fully to the pelvic floor. (From Uhlenhuth, E., Wolfe, W. M., Smith, E. M., and Middleton, E. B.: Surg., Gynec. & Obst. **76**: 148, 1948.)

It is not uncommon for both uterovaginal and rectal prolapse to coexist. These traction hernias constitute by far the larger group, and there is an abnormal cul-de-sac protrusion in many second-degree prolapses and in all third-degree descensus. This protrusion would appear to be the direct result of descent of the uterus and vagina causing traction on the anterior peritoneal wall of the cul-de-sac.

Some criticism has been directed against the nomenclature of pouch-of-Douglas hernia in that while the cul-de-sac is normally a hernia-like protrusion, the simple extension of such a protrusion cannot convert it into a true hernia. Be this as it may it is difficult to improve on this nomenclature. Meigs goes so far as to say that there is no such thing as a hernia of the pouch of Douglas

except when it prolapses through the anus and becomes a prolapse of the rectum. This, possibly, is strictly true. In such cases, the congenital type of hernial orifice appears as a narrow-necked protrusion of the cul-de-sac which is directed toward the anterior rectal wall. It may enlarge to considerable dimensions, and would aptly be described as a true hernia of the pouch of Douglas, i.e., a true hernia emanating from a natural hernia. I hope it is appreciated that in this contribution the term, enterocele, embraces all abnormal protrusions of the cul-de-sac.

The association of rectocele with enterocele was stressed by the late George Gray Ward of this city as far back as 1922. Moschowitz in 1912 demonstrated that laxity in this area was frequently associated with rectal descent, and of course the association of rectocele, enterocele, and rectal prolapse is well recognized.

Fig. 4.—Dorsal dissection of a woman 35 years old. The coccyx, levator ani, and rectum have been removed. The dorsal and ventral leaves of the fascial capsule of the rectum were incised longitudinally; on the left side these have been removed while on the right they were reflected to the right. The rectovaginal septum is seen from its dorsal aspect. The muscular wall of the vagina is visible through a longitudinal slit in the rectovaginal septum. (From Uhlenhuth, E., Wolfe, W. M., Smith, E. M., and Middleton, E. B.: Surg., Gynec. & Obst. 76: 148, 1948.)

Rectocele or Enterocele?

It is frequently easy to distinguish the presence of a cul-de-sac hernia with or without the presence of a rectocele, and the presence of palpable coils of ileum which are reducible is not uncommonly demonstrable with large enteroceles. In many cases, however, such distinction is extremely difficult. Com-

bined rectovaginal examination in the standing position, while the patient is asked to strain, may make an accurate diagnosis possible, and in a few instances there is a visible transverse sulcus between the lower extremity of the cul-de-sac above, and the rectocele protrusion below. In a few cases accurate diagnosis is impossible until the rectovaginal space is operatively opened and the sac exposed to view. Except in the case of so-called true narrow-necked congenital hernias, the elongated sac is always adherent to the posterior vaginal wall, and the junction of enterocele and rectocele is marked by the presence of extraperitoneal fat.

Prevention of Enterocele

During the course of an abdominopelvic operation inspection of the cul-de-sac may reveal the presence of a true congenital hernial dimple or small sac. Closure of this by peritoneal oversew is a worth-while procedure. Likewise the finding of an abnormally deep or wide pouch of Douglas may be an indication either to excise or to obliterate the protrusion by circumferentially placed catgut sutures, both procedures being followed by approximation of the uterosacral folds with interrupted sutures. In both instances the operation will have prevented the subsequent development of a symptom-producing enterocele.

The Principles of Cure

Whether the hernia be a traction or a pulsion protrusion and irrespective of its being congenital or acquired, the principles governing the treatment of hernias generally must be applied. The sac must be exposed, opened, emptied of its contents, ligated, and excised. The hernial orifice must be effectively occluded by uterosacral ligament approximation and, in addition, it is preferable that further support be added from below by approximation of the upper portions of the cardinal ligaments or by a careful high repair of the prerectal fascia, with care being taken that the uppermost sutures in this fascia also include the posterior wall of the isthmus uteri just below the attachments of the uterosacral ligaments to the uterus. The prerectal fascial repair is of especial importance in the case of rectocele associated with enterocele.

One cannot overstress the importance of the association of hernia of the pouch of Douglas with uterovaginal descent, and too often a small enterocele, or a high posterior weakness is unnoticed in the course of a plastic vaginal repair. Failure to observe this association all too often results in a cure of the uterine and vaginal descent, with the persistence of, and further development of, an annoying enterocele whose symptoms are as troublesome as those of the pre-existing prolapse. In my first visit to this country some fourteen years ago I was impressed by the efficacy of high cardinal ligament and prerectal fascial approximation demonstrated by Bullard at the Woman's Hospital in such cases, and since then have frequently adopted this procedure. On occasions, however, the tension is considerable, and in such cases there is some danger of vault narrowing.

The Peritoneal Sac and Hernial Orifice

It is important to excise this as completely as possible. Sease has recommended inversion of the sac and simple ligature, but on two occasions I have seen a peritoneal cyst result, which in both instances required subsequent excision, and I have abandoned this. In some cases both the hernial orifice and the neck of the sac can be brought together by a single purse-string suture which includes uterosacral ligaments, anterior rectal wall, and posterior aspect of the isthmus of the uterus. The redundant peritoneal protrusion is then excised. Usually, however, I feel it is a preferable procedure to approximate the uterosacral ligaments from anterior rectal wall posteriorly to uterine isthmus anteriorly by interrupted sutures of fine silk or chromic catgut. Sjövall of Sweden has described a method of posterior vaginal fixation of the uterus, a posterior interposition operation, whereby the body of the uterus is fixed posteriorly to occlude a large uterosacral hiatus with enterocele. I have to date not encountered a case in which I have considered this procedure necessary.

A.   B.

Fig. 5.—Exposure of the hernial sac and approximation of the uterosacral ligaments. A, With amputation of cervix as in the Manchester operation; B, without amputation of cervix. (Courtesy of J. W. A. Hunter, Manchester.)

In 1942 Phaneuf presented a paper before the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, showing excellent results in a personal series, and in several instances he employed colpocleisis in some large hernias where there was a contraindication to laparotomy. As will be seen later, I have employed the abdominal approach with cul-de-sac obliteration described by Marion in 1909 and slightly modified by Moschowitz in 1912.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 6.—Simple approximation of the uterosacral ligaments after suture to the pubocervical fascia on either side (diagrammatic).
Fig. 7.—Approximation of the uterosacral ligaments with suture of the anterior extremities to the subpubic ligament (diagrammatic.)
Fig. 8.—Crossing of the uterosacral ligaments and fixation to the broad ligament pedicles of the opposite side (diagrammatic).

In some instances I have employed a combined vaginoabdominal approach to cure the more intractable and difficult enteroceles.

Clinically, hernia of the pouch of Douglas may be conveniently classified into the following two groups:
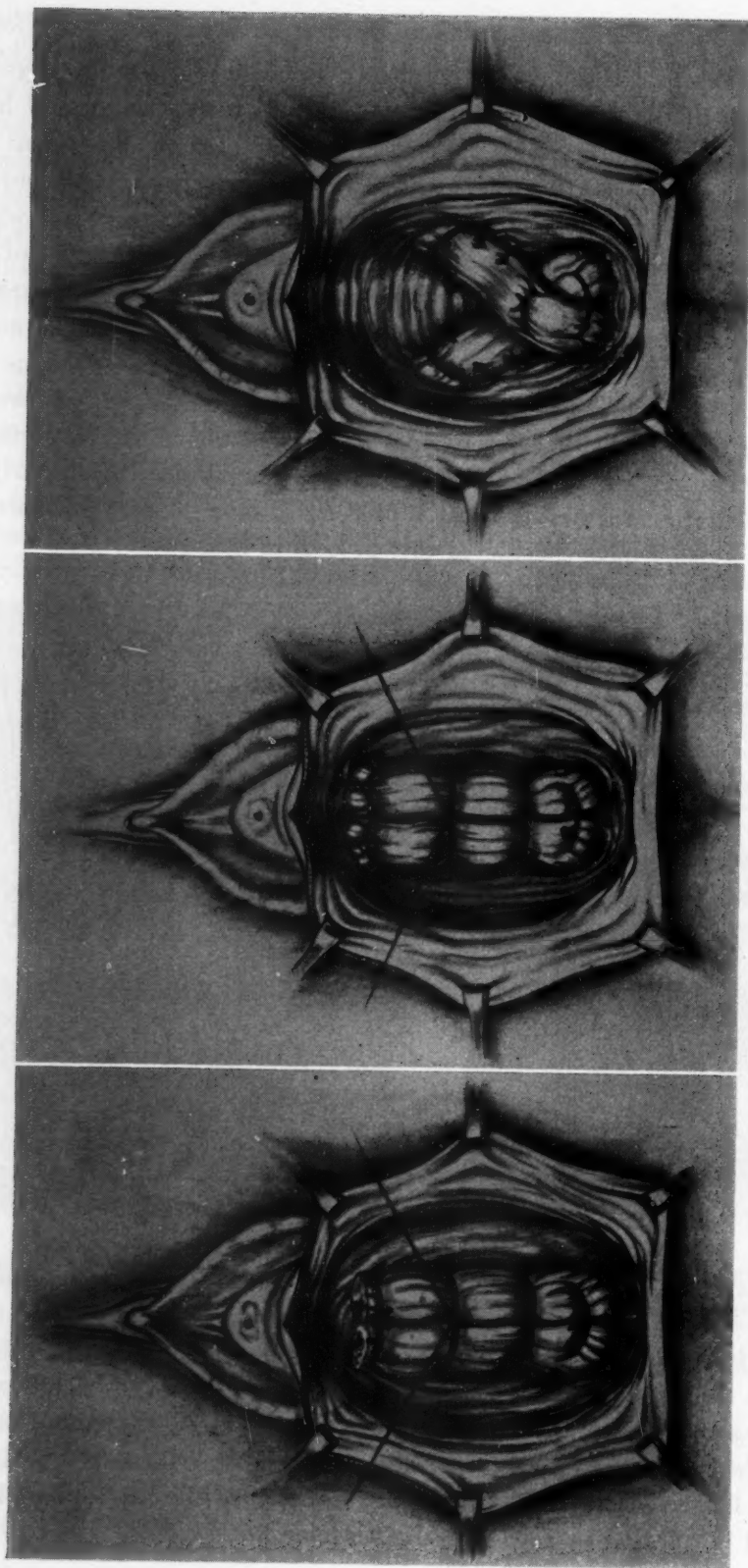
1. Enterocele associated with uterovaginal descent.
2. Enterocele with or without rectocele formation.

This latter group largely includes patients in whom an otherwise successful cure of uterovaginal descent has been accomplished.

These comments on each group are those I made in 1949 in London, as with a further two years' experience I see no reason for modifying them.

1. Enterocele Associated With Uterovaginal Prolapse

The operative treatment of this, the largest group, is by the vaginal route. The surgeon has the choice of performing a Manchester type of operation with an associated cul-de-sac repair or a vaginal hysterectomy with repair. It will be seen later in the statistical tables that I have preferred the Manchester type of operation on 93 occasions. This proportion will be questioned by those who are enthusiasts for vaginal hysterectomy, but I have performed vaginal hysterectomy and repair for prolapse with enterocele only when there has been a symptomatic or organic indication for removal of the uterus or where there has been present procidentia with complete eventration of the vagina down to the mucocutaneous junction.

During the course of the Manchester type of operation, immediately after the amputation of the cervix, the cervical stump is retracted vertically upward, the peritoneal pouch is carefully dissected, opened, and freed up to the level of the uterosacral ligaments, which are seized on either side by Allis forceps. The sac is transfixed and ligated with No. 2 catgut at this level, and the uterosacral ligaments are then approximated by three or four accurately placed No. 3 silk sutures. The cervical, parametrial, and anterior vaginal repairs are then completed. A high posterior repair is then performed up to the level of the cervical stump. The prerectal fascia is pleated and the uppermost stitch includes the posterior wall of the supravaginal cervix or uterine isthmus, and the posterior colpoperineorrhaphy is completed by the usual vaginal wall and levator muscle approximation.

When vaginal hysterectomy is the method adopted, the essential steps for the cure of the enterocele are the excision of the full extent of the peritoneal protrusion, careful peritoneal closure together with approximation of the uterosacral ligaments. This approximation may be accomplished in a variety of ways as described by Ward, Kennedy, Campbell, and Palmer, or as described in the Mayo-Ward operation, or in the recent publication of Veenboer and Kooistra. I have performed several variations of procedure in such cases:

A. Simple approximation of the ligaments in the midline from before backward, the posterior suture taking in the anterior rectal wall.

B. Crossing the uterosacral ligaments with suture of each to the broad ligament of the opposite side, with careful closure of the small posterior hiatus.

C. Simple approximation of uterosacral ligaments as in A, with suture of each ligament to the pubocervical fascia of its own side (Campbell and Kennedy). If the ligaments be sufficiently long the anterior extremities may be sutured to the subpubic ligament on either side (Veenboer and Kooistra). In my experience both these procedures tend to shorten the vagina.

Fig. 9,A.   Fig. 9,B.
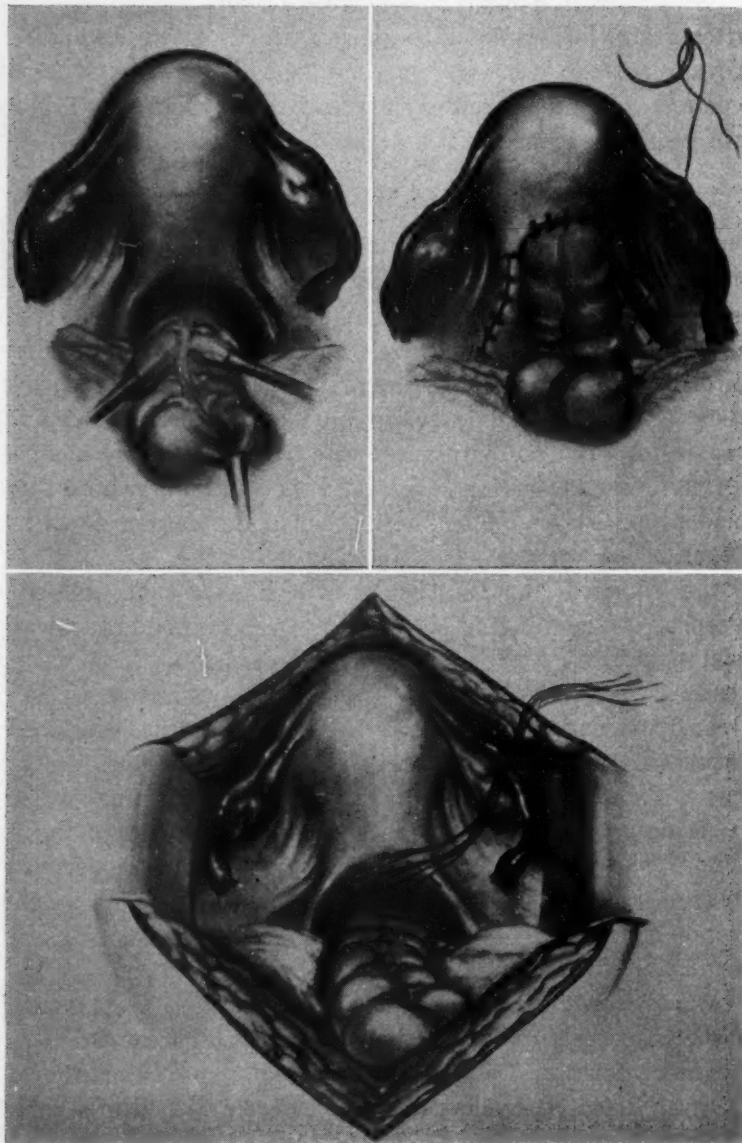

Fig. 10.

Fig. 9, A and B.—Exclusion of cul-de-sac. (After Curtis.)
Fig. 10.—Obliteration of cul-de-sac. (After Moschowitz.)

I would agree with Phaneuf, Counseller, and others that the usual uterosacral approximation performed with the Mayo-Ward operation leaves a distinct weakness posteriorly, and the recurrence of enterocele in such cases has been estimated as high as 10 per cent.

2. Enterocele With or Without Rectocele, Often Following an Otherwise Successful Cure of Uterovaginal Prolapse

It will be seen later that this group comprises 63 patients in my series. Of this number 38 patients had been subjected to a previous vaginal repair for prolapse and three in addition had been treated by vaginal hysterectomy and repair for uterovaginal descent.

All cul-de-sac hernias with associated rectocele formation must be surgically approached via the vaginal route, and the same principles for cure obtain, high posterior exposure, excision of sac, uterosacral ligament approximation, and prerectal fascial and levator repair.

A.   *B.*

Fig. 11, *A* and *B.*—Obliteration of cul-de-sac after excision of peritoneum of the pouch.

Most enteroceles without associated rectocele can be similarly cured via the vaginal approach, but on eleven occasions I have operated on such patients without associated rectocele via the abdominal route. The procedure is that suggested by Marion in 1909 and modified by Moschowitz in 1912. On most occasions I have, after opening the abdomen, excised the peritoneal pouch below the level of the uterosacral ligaments and have approximated the ligaments with obliterative interrupted No. 3 silk sutures, the posterior of which transfixes the peritoneum of the anterior rectal wall, while the anterior transfixes the posterior wall of the uterine isthmus. A fine catgut repair of the peritoneal edges is then performed, excluding the uterosacral ligaments from the celomic cavity. Otherwise I have obliterated the pouch without peritoneal excision, using the usual technique.

The indications for this procedure are limited, and I find I have performed this on only four occasions for enterocele alone, while in addition on seven occasions I have effected this repair during the course of laparotomy primarily for the performance of a separate intra-abdominal procedure.

On four occasions I find I have resorted to a combined vaginoabdominal approach. All four were patients with very large pouch of Douglas hernias

associated with rectoceles, and all had previously been subjected to hysterectomy, three vaginal and one abdominal total hysterectomy. This type of case presents a difficult problem. After a high posterior fascial and levator repair had been effected, the abdomen was opened, the whole peritoneal sac excised, and the cavity obliterated by approximation with silk of the remains of the uterosacral ligaments from the anterior rectal wall posteriorly to the scar of the vaginal vault anteriorly. All four showed gratifying postoperative results.

I have not included in the series two elderly patients with recurrent vaginal eventration associated with enterocele following vaginal hysterectomy, as they were both treated by vaginectomy and colpocleisis. Both operations were performed just before this series was begun, and I doubt if I shall again have occasion to resort to this deforming procedure.

TABLE I. HERNIA OF THE POUCH OF DOUGLAS

Total personal patients, 1939-1951 inclusive,	167

TABLE II.

Age Incidence.—	
Average age of patients	57 years
Oldest	71 years
Youngest	36 years
Decade Incidence.—	
30-40 years	8
40-50 years	56
50-60 years	72
60-70 years	30
Over 70	1

TABLE III. PARITY

Parous	151
Nulliparous	16

TABLE IV. PREVIOUS OPERATIVE INTERFERENCE OF ASSOCIATED IMPORTANCE

a. Plastic vaginal repair of uterovaginal prolapse	51
b. Vaginal operation for enterocele only	4
c. Ventrofixation	14
d. Operation for severe rectal prolapse	4
e. Vaginal hysterectomy and presumably repair	7
f. Le Fort operation	1
g. Total abdominal hysterectomy	4
h. Supravaginal hysterectomy	4

I should like to present the relevant details of a series of 167 operations for the cure of posterior vaginal hernia, all performed by me personally between the years 1939-1951 (Tables I to VII). In the main I have followed the scheme of Phaneuf in their presentation, but my series is more recent than that of Phaneuf, and represents work done during the past 12 years only. Of necessity many are very recent cases, and this in some measure accounts for

the apparently good results obtained. I have little doubt that at least some of these immediate cures will prove to be eventual failures. The results are also affected by the fact that a personal follow-up by interview and examination was not possible in a considerable number of cases. Follow-up by questionnaire was employed with these, but the fallacies of a questionnaire follow-up are such that the results shown must appear to be somewhat unreliable.

TABLE V.   METHOD OF TREATMENT EMPLOYED IN 167 CONSECUTIVE PERSONAL CASES

1. Repair of enterocele with concomitant cure of uterovaginal prolapse	104
a. Manchester operation or modification, associated with	
cure of enterocele	93
b. Vaginal hysterectomy with repair and cure of enterocele	11
2. Vaginal repair of enterocele alone or with rectocele only	48
a. Repair of enterocele alone	31
(26 of the above patients had previous operative	
vaginal repair for uterovaginal prolapse)	
b. Repair of enterocele with rectocele	17
(Twelve of these patients had previous vaginal repair)	
3. Abdominal approach with repair of enterocele	11
a. Repair of enterocele alone	4
b. Repair of enterocele in course of other abdominal procedure	7
(Total hysterectomy 5, ovarian cystectomy 1,	
ventrosuspension 1)	
4. Combined abdominovaginal repair for recurrent enterocele and	
rectocele following previous hysterectomy	4
a. Vaginal hysterectomy	3
b. Total abdominal hysterectomy	1

TABLE VI

Mortality.—One death in series on the tenth postoperative day	
Cause of death.—Peritonitis	
Morbidity.—	
a. Urinary infection necessitating treatment by the	
administration of alkalis and sulfonamides	41
b. Urinary or fecal fistulas	Nil
c. Secondary hemorrhage necessitating vaginal packing	2
d. Postoperative thrombophlebitis	3
One associated with pulmonary embolism (recovered)	
e. Rectovaginal hematoma	3

TABLE VII.   RESULTS OF FOLLOW-UP, 167 PATIENTS

1. Patients examined	117
a. Cured and symptom free	111
b. Recurrent enterocele	1
c. Peritoneal cyst (since excised)	1
d. High dyspareunia (not present before operation)	4
2. Questionnaire replies	34
a. Symptom free	28
b. High dyspareunia	2
c. "Severe" backache	3
d. Subsequent operation for rectal prolapse	1
3. Untraceable (including one death)	16

From the tables it will be seen that I have performed relatively few vaginal hysterectomies with concomitant repair for pouch of Douglas hernias for the

reason before stated, that it is my practice to reserve vaginal hysterectomy for those cases in which there is a definite indication to remove the uterus because of hemorrhage or the presence of relatively small fibroids. An exception to this rule is made in patients over 40 years of age with complete eventration of the uterus and vagina. I feel, however, in retrospect, that my incidence of vaginal hysterectomy is probably too low. There is no doubt, however, that the approach afforded by the Manchester operation enables one to cure both enterocele and uterovaginal prolapse, even when the enterocele is large and the prolapse severe in degree. I feel that the end result of the Manchester repair, in my hands, offers a more stable repair than do vaginal hysterectomy and repair. Often this is attributable to the fact that some operators consider the vaginal hysterectomy the important factor in cure of prolapse, whereas it should be merely an incident in the course of a careful repair.

In conclusion, may I state that congenital elongation of the pouch of Douglas is more common than is generally appreciated. Many such protrusions are symptomless until a downward intestinal thrust manifests itself or until a ventrofixation be performed. Acquired enteroceles may be "traction" or "pulsion" hernias, and it is probable that a pulsion enterocele may cause utero-vaginal descent just as a traction enterocele may be the result of such descent. The majority of posterior vaginal hernias are associated with uterovaginal prolapse, and if in every plastic vaginal repair the operator looked for and repaired high posterior laxity or small enterocele formation, the incidence of subsequent clinical enterocele would be markedly diminished. Indeed, over one-fourth of the patients in my series would have avoided subsequent operative intervention. Whether the surgical approach be vaginal, abdominal, or a combination of both, the same principles of cure obtain, excision of the sac, closure of the neck of the sac, uterosacral ligament approximation, combined preferably with a prerectal fascial repair. I close as I did in London in 1949: "Only a strict adherence to these principles will eliminate the so-called post operative 'recurrent' enterocele, which in the vast majority of cases is not recurrent but in fact a 'neglected' enterocele."

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104 HARLEY STREET, W. 1

EXPERIENCE WITH THE Rh FACTOR IN 1,000 CONSECUTIVE WHITE OBSTETRICAL PATIENTS*

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AS THE title indicates, this is a review of 1,000 consecutive Rh determinations in private practice. We think it worth while to record the findings in such a series, as the ramifications of the problem can best be studied by the pooling of our collective experiences. We shall not discuss the history of the discovery of the Rh factor, nor the scientific and theoretical aspects of the subject, as these matters are amply covered in the literature. We use the designation Rh_0 (D) to designate the factor found in approximately 85 per cent of the white race; this designation embraces both the American and the English methods of classification.

The tests on these patients were all performed in the laboratory of Dr. J. W. Davenport, many of the determinations being made by him personally, the others under his direct supervision. In doubtful cases, blood samples were sent to Dr. Philip Levine for his opinion. We feel that it is highly important that very rigorous attention be paid to all details of the tests, that the sera used be the best obtainable and be checked frequently, and that various additional tests as checks be performed when indicated. In our early experience we found that erroneous results followed the use of substandard sera and the use of sera which had become contaminated with bacteria. It appears to us to be particularly unwise and unsafe for a physician with a laboratory in connection with his office to attempt Rh determinations, or to have them made by a technician. The techniques of the various tests are so exacting that errors might creep in unless every precaution is taken, with serious results, especially if blood transfusion be involved.

It is our practice to obtain an Rh determination on every new patient early in pregnancy. The blood is tested for the Rh_0 (D) and for the Hr' factors, and the type is also determined. Tests are also made for Rh_0 and Hr' agglutinins and for blocking antibodies, and at times for the Rh' and Rh" factors. From a practical point of view, the Rh_0 (D) factor is the important one, being present in about 85 per cent of white persons. We have never experienced an instance of Hr' incompatibility; Davenport[1] has observed only two in many thousands of cases studied by him.

If the patient is found to be Rh_0 (D) positive, the husband and children (if any) are not tested. If she is negative the husband is tested and children (if any) are tested. If he is positive the mother's blood is also tested for agglutinins and blocking antibodies. If the husband is negative, he can father only negative

children, hence isoimmunization cannot occur, further tests are not needed
If the husband is Rh_0 (D) positive, he might be heterozygous and capable of
fathering either positive or negative children, or homozygous and all his children
will be positive.

If the patient is a primigravida and the husband is Rh_0 (D) positive, and
there is no history of her having received blood by transfusion or intramuscularly,
the risk of the presence of isoimmunization is practically nil and further tests
are not necessary in this pregnancy. The baby's cord blood is tested at delivery.
If she is a primigravida with a history of blood administration, the donors, if
available, are tested. If they are positive, or are not available for testing, tests
for agglutinins and antibodies are performed and are repeated at the sixth or
seventh month, and again at the eighth month. The same testing is done if the
patient is a multigravida with a positive husband (or in case she is married the
second time to a positive husband and the Rh of the first husband is not known).
Most of our Rh_0 (D) negative patients are tested again six weeks post partum,
and in one case a patient previously free was found to first manifest antibodies
at this time. No explanation has been advanced for this development. Patients
in whom antibodies were first found late in pregnancy have frequently lost them
by the sixth week post partum; if not, they are tested again in three to six
months.

Clinically, it appears that women showing blocking antibodies early in
pregnancy are very likely to deliver affected children, especially if the titer rises
in the later months. If the agglutinins disappear as the blocking antibodies
increase, the prognosis seems worse. This is by no means an invariable rule, as
many of our patients who have manifested these findings have delivered healthy
Rh-negative children. The antibody change must have been caused by some
other factor. If the antibodies persist throughout the interval between two
pregnancies, the prognosis for the unborn child is particularly ominous, unless
the child happens to be Rh negative. We feel that isoimmunization produced by
transfusion of Rh-positive blood is more severe than that caused by pregnancy,
but this impression may be erroneous. As is well known, the isoimmunization
may occur in the second and/or subsequent pregnancies, or it may not develop at
all. Because of the many variables involved, it can be seen that the prognosis
for the child is in most instances difficult to evaluate.

It is sometimes stated that Rh-negative women are more prone to abortion
than their positive sisters. Of the 139 in this series with positive husbands, 19
gave a history of abortion, i.e., 15 per cent of the total number. Of the 21 women
sensitized to a greater or less degree, 3 had a history of abortion; again, 15 per
cent. This figure is less than the 20 or 25 per cent incidence generally accepted
as the average for childbearing women.

Of the 1,000 women under consideration, 823 (82.3 per cent) were found
to be Rh_0 (D) positive and hence presented no problem; 177 (17.7 per cent)
were Rh_0 (D) negative; a proportion a little higher than the 15 per cent gen-
erally accepted as the correct figure for the white race (Table I). Of the 177
Rh_0 (D) negative patients, 23 were married to Rh_0 (D) negative men, hence
there was no possibility of isoimmunization from pregnancy, and no chance of
fetal damage even if transfusion from a positive donor had occurred, as all chil-
dren of such unions are Rh_0 (D) negative. In 15 instances the husbands were
not tested, usually in the early years of this series, in case the wife was a
primigravida with no history of previous blood administration. We soon estab-
lished the principle of testing the husband of every Rh_0 (D) negative woman.
Thus we have a total of 139 Rh_0 (D) negative women with positive husbands
(Table II).

Of these 139, in 53 there was no possibility of isoimmunization previous to
the pregnancy. Sensitization produced by the first pregnancy, as is well known,

TABLE I.

Total number of women examined	1,000
Number found to be Rh_0 (D) positive	823 or 82.3%
Number found to be Rh_0 (D) negative	177 or 17.7%

TABLE II.

Number of Rh_0 (D) negative women	177
Those with Rh_0 (D) negative husbands	23
Husbands not tested (mainly in case of primiparas with no history of blood administration)	15
Women with Rh_0 (D) positive husbands	139

occurs gradually toward the end of gestation, and no fetal damage can be produced in the pregnancy under consideration. In 86 women there was a possibility of previous isoimmunization, as they were either multigravidas (84) or primigravidas with history of previous blood administration[2] (Table III).

TABLE III.

Rh_0 (D) negative women with positive husbands	139
Isoimmunization a possibility	86
Not to be expected and not found (primigravidas with no transfusion history)	53

Five of these 84 multigravidas had been transfused in their first or subsequent pregnancies, two from known positive donors, in the other three instances the status of the donor could not be ascertained. As their husbands were positive, the responsibility for fetal damage could not be placed.

Of these 86 patients, isoimmunization severe enough to cause fetal damage was found in 14 (approximately 1 in 6). In 7 other women with antibodies there were no fetal complications. Antibodies were found late in pregnancy and of low titer in three of these patients who delivered healthy Rh_0 (D) positive babies. The other 4, with high and rising titers in 3, delivered healthy Rh-negative babies in these three instances; the fourth with a high but unchanging titer, aborted at the sixth month (Table IV).

TABLE IV.

Rh_0 (D) negative women with possible isoimmunization	86
Antibodies present and marked fetal damage	14
Antibodies present with no fetal damage	7
No antibodies and no fetal damage	65

The 14 women who were immunized to varying degrees were delivered of 18 babies, 6 by cesarean section and 12 vaginally. Of these 18 infants, 5 are living and normal, 1 is living and mentally deficient, 5 were stillborn at or near term, 1 was lost by abortion at the sixth month, and 6 died in the neonatal period (Table VI).

TABLE V.

Women presenting serious degree of isoimmunization	14
Total pregnancies	18
Children living and normal	5
Children living and mentally abnormal	1
Lost by abortion at sixth month	1
Stillborn	5
Neonatal deaths	6

TABLE VI. DETAILS OF DELIVERY OF THE 18 BABIES (GROUP IN SERIOUS CONDITION)

	LIVING	STILLBORN	NEONATAL DEATHS	TOTAL
Vaginal delivery	5	2	4	11
Cesearean section (3 repeats, 2 for erythroblastosis, 1 for toxemia)	1	3 (Hydrops)	2	6
Abortion at sixth month		1		

It is fair to ask if any of the 11 babies in this group that were lost might have been saved by other methods of treatment. Three of the stillborn infants and two of those lost neonatally were of the hydrops type; the mortality in this type is universally reported as 100 per cent. Delivery by induction of premature labor or by cesarean section at the eighth month would hardly have saved them; the condition was well established in one born at the seventh month. The two other babies in the stillborn group died in utero several days before birth; these deliveries were in the early years of Rh study; possibly induction of labor at the eighth month might have been of value had the condition been recognized. The diagnosis in each case was established by autopsy of the child and subsequent blood studies on the mother. Of the 4 babies not of the hydropic type who died in the neonatal period one infant was delivered by cesearean section at 8 months, one by section at 8½ months. Earlier delivery would have increased the risk from prematurity. These babies lived 3 and 5 days, respectively. The other 2 were born at term; one lived 12 hours, the other 5 hours. The latter was the only case of death of the four treated by replacement transfusion; death occurred just at the end of the transfusion and could not be explained clinically or by autopsy. It was our opinion at delivery (and still is) that the transfusion should have been given immediately after birth, but the pediatrician and the serologist did not agree; rapid development of jaundice caused a change of opinion. In the light of our present knowledge, we feel that the chances of the 3 other infants would have been much better with replacement transfusion (not developed early enough for them, however), but we do not feel that earlier delivery in any of these cases would have been of any avail. Mollison[3] is of the opinion that if the fetal cord blood has hemoglobin of 16 Gm. or more, no treatment is needed; if less, active measures are indicated.

TABLE VII.

Antibodies (maternal) present but no fetal complication	7
Rh_0 (D) negative babies at term and healthy (with rise in maternal blocking antibody titer)	3
Rh_0 (D) negative fetus, miscarried at sixth month (blocking antibodies in maternal blood)	1
Rh_0 (D) positive babies, at term and healthy (low maternal antibody titer or late development of antibodies)	3

Note.—Two patients delivered by section; one because of rising antibody titer (negative baby), one repeat. Babies in this group required no treatment.

TABLE VIII. TREATMENT OF THE 12 LIVEBORN BABIES (GROUP SEVERELY ILL)

Replacement transfusion		4
Living	3	
Died	1	
One or more small transfusions		7
Normal living	2	
Living and mentally retarded	1	
Died	4	
No treatment, hydropic, died in one-half hour		1

Is there any prenatal maternal treatment which offers hope of desensitizing the mother (thus benefiting the fetus) or of aiding the baby by the transplacental route? Our experience (and that of everyone else) is limited, but up to the present we are forced to answer, no. We have tried various methods without satisfactory results. Methionine, as suggested by Philpott,[2] was given to 3 patients, the idea being that thereby the fetal liver might be protected to some extent. Results were: one Rh-positive baby lost, one Rh-negative baby lived, and one Rh-negative baby lost by abortion at the sixth month. However, his reasoning appears logical, and further experience might prove more convincing. Hapten was also given to two of the above patients; one delivered an Rh-positive baby who died in 4 hours, one aborted as noted above. In the first instance, no reduction in antibody titer was noted. The same negative results have been noted by others in our city and elsewhere. Ethylene disulfonate, as suggested by Kariher,[4] was administered to one patient with no result; the baby was lost. We have not had the opportunity of trying the combination of vitamin K and progesterone, as recommended by Hoffman and Edwards,[5] but their small series of three cases can only be indicative of possible worth-while results. Of course, these results are of no value statistically, but they reinforce the opinions of others. Patients must be made to understand that the sanguine opinions of popular magazines in favor of the combination of premature labor and replacement transfusion are not justified by the facts.

We have, therefore, no definite conclusions to offer. We do not feel that induction of labor or cesarean section three or four weeks ahead of the calculated term date has been proved to be of sufficient value to offset the risk of prematurity. A rising antibody titer has very little significance; it has been noted with Rh-negative babies. We feel strongly that the hydrops baby cannot be saved and that the condition is established early; however, the reported x-ray halo has not been apparent in any of the films seen by us. If we could be warned by some tests that a fetus of the anemic or icteric type was being progressively damaged, premature termination of the pregnancy might help. So far, there is no way of arriving at such a conclusion. Hence, we feel that we should carry the pregnancy to term and normal labor (unless other indications are present), using methionine, vitamin K., etc., if we feel that they are of any possible value, and then should treat the baby by replacement transfusion, if indicated, or by other methods that may appear proper. If a woman has lost a baby previously due to the Rh factor, we advise her against further pregnancies unless her husband is definitely heterozygous for the Rh factor, in which case she has a 50 per cent chance of having a healthy Rh-negative child. We can only hope that more definitive methods will soon be evolved.

References

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Discussion

DR. NEWELL PHILPOTT, Montreal, Canada.—Dr. King is to be congratulated on this study of obstetrical cases which are complicated by the Rhesus factor.

At the Royal Victoria Hospital we are still using methionine with the thought that it is a liver protective for the unborn fetus; we think it has some beneficial effect in this regard.

Since 1948 we have had a special Rh Factor clinic which only Rhesus factor negative individuals attend. In this way they are closely observed and they afford excellent material

for study. In addition, we obtain a large number of Rh-negative women who are willing to be placed on our blood donor list. Consequently we are never short of Rhesus-negative blood in the hospital blood bank.

Rhesus factor negative women were examined in 1949 and 1950 as follows:

Total number	1,262
Number definitely immunized	55
Deduct referred patients	5
Total delivered in Royal Victoria Hospital	50
Abortions, induced (1), spontaneous (4)	5
Fetus died in utero, at 8 months	2
Live babies, 37 weeks plus	43
Rh negative normals	3
Hemolytic disease	40

BABIES WITH HEMOLYTIC DISEASE, 1949-1950

	NO.	DEATHS
Died in utero	2	2
Untreated cases	5	2
Ordinary transfusions	24	0
Replacement	11	3
Mortality incidence		15.5%
Kernicterus in survivals		None.

There are only three points to emphasize: First, blood transfusion is the only form of treatment which produces consistently good results. Second, in those babies who are born from immunized mothers and who do not receive prompt treatment when indicated, the mortality is unduly high. Third, when treatment is prompt and adequate, the various disturbing sequelae such as spastic paralysis and imbecility very rarely occur in the survival cases.

DR. KING (Closing).—Some of the fetal deaths we have had I felt were due to hesitancy of the pediatrician in backing us up in thinking a transfusion should be done. In one particular case the mother had presented difficulty in her previous pregnancy; that baby was treated successfully by replacement transfusion twelve hours after delivery when it went rapidly downhill. At the next delivery, the pediatrician and the serologist said to wait. We waited three hours and the baby rapidly grew worse and became jaundiced. Replacement transfusion was done and the baby died at the end of it. I felt that the baby should have been transfused promptly after delivery.

We have not had as much success in finding the umbilical vein open when the replacement transfusion is delayed. In this particular baby, four hours after birth we could not transfuse in the umbilical vein because it was closed; it was necessary to transfuse through the femoral vein.

Our one suggestion is that these babies be carefully classified as to whether they are severely or slightly ill and if the illness is severe and there is a bad history in the mother in a previous pregnancy it would be best to give the baby prompt replacement transfusion.

STUDIES OF BLOOD OXYGEN SATURATION AND CAUSES OF DEATH IN PREMATURE INFANTS*†

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THE human fetus is able to live and grow in utero with arterial blood that is approximately 50 per cent saturated with oxygen. During the first few minutes of extrauterine life, the infant makes remarkable adjustments to his new environment. One extremely important change is the increase from approximately 50 per cent to 90 per cent or mcre blood oxygen saturation. In the normal full-term infant this adjustment usually is completed 30 minutes to 3 hours after delivery.[17] In a previous study we demonstrated the depressive effect of maternal general anesthesia on the physiologic adjustment of infant blood oxygen levels during the early hours of life.[19] The purpose of this paper is twofold: to present studies on the effect of prematurity on neonatal blood oxygen saturation and to analyze the causes of infant deaths associated with prematurity.

In an effort to reduce fetal deaths at the Colorado General Hospital, the Department of Obstetrics and Gynecology, in conjunction with the Department of Pediatrics, routinely makes a critical study of each infant death that has occurred on the obstetrical service. Since premature birth has been associated with one-half of our fetal deaths, attention has been focused upon the problem of prematurity. It has been our practice to view each infant death in the light of obstetrical contributing factors: maternal disease, prolonged or deep anesthesia, excessive analgesia, traumatic labor or delivery. In joint teaching conferences we have tried to assess factors of preventability. Autopsy findings have been correlated with the obstetrical course of the mother and the clinical course of the infant.

Methods and Materials

Between July 1, 1946, and Jan. 1, 1951, 465 infants of less than 2,500 grams birth weight were born alive on the obstetrical service of the Colorado General Hospital. During this time general anesthesia has been avoided in almost all deliveries of premature infants; maternal analgesia has largely been withheld; specialized medical and nursing care has been available. Our incidence of prematurity was 11.7 per cent during this period. Thirty-nine deaths occurred among infants weighing between 1,000 and 2,500 grams at birth. Thirty-eight of these 39 infants have been carefully examined for anatomical causes of death.

The experimental portion of this paper includes a report of capillary blood oxygen determinations performed on 50 premature infants who weighed between 1,000 and 2,500 grams at birth, only one of whose mothers had received a general anesthetic agent. These are compared to blood oxygen saturation values found in a study of 10 full-term infants whose mothers received no general anesthesia.[19] The determinations were made at birth, at one-half hour, and at one hour of life. The infants (premature and full-term) were placed in a conventional incubator containing 50 to 60 per cent oxygen as soon as respirations became established. The determinations were made by a micro-method described by Roughton and Scholander.[16] These authors demonstrated this method to be accurate when compared to the Van Slyke method performed on aerated blood. Two-hundred seventy-eight separate determinations were done on 50 premature infants, each determination being performed in duplicate. Lundsgaard and Möller[10] have shown that determinations done on the capillary blood of subjects agree with simultaneous samples taken from the arterial blood.

NEONATAL MORTALITY FOR 465 PREMATURE INFANTS ACCORDING TO WEIGHT GROUPS

WEIGHT IN GRAMS	LIVE BORN	PER CENT OF TOTAL	NEONATAL DEATHS	PER CENT OF TOTAL DEATHS	MORTALITY RATE
Below 1,000	26	5.6	23	37	88.5%
1,000 – 1,499	40	8.6	16	26	40.0%
1,500 – 1,999	95	20.4	13	21	13.7%
2,000 – 2,499	304	65.4	10	16	3.3%
Total	465	100.0	62	100	13.3% (Average)

Results

Premature Infant Neonatal Survival Rates.—The neonatal death rate among infants weighing less than 2,500 grams at birth was 13.3 per cent. If those infants weighing less than 1,000 grams at birth are omitted from the calculation, the premature infant neonatal mortality rate was 8.8 per cent. The rates for premature infant neonatal survival at the University of Colorado compare favorably with the excellent results reported by Calkins[4] and by Masters and Ross.[13]

Postmortem Findings as Related to Obstetrical History and Clinical Course of Infant.—Autopsies were performed on 38 of 39 premature infants who were in the weight group of 1,000 to 2,500 grams. The autopsy findings are summarized as follows:

Hydrops fetalis or kernicterus	3
Congenital deformities	5
Sepsis	4
Lacerations, falx or tentorium	7
Intracranial hemorrhage	7
Hyaline membrane, alone	7
Focal hemorrhages of asphyxia	2
Atelectasis	3
	38

Autopsies were completed on those infants of less than 1,000 grams birth weight, but these are not being reported now.

Three deaths were due to hydrops fetalis or kernicterus. Five more were associated with congenital abnormalities of which four were incompatible with continued life.

Four deaths were due to sepsis. Two of these premature infants were born of mothers having long-ruptured membranes. The mothers had not received

antibiotics during the prenatal period of ruptured membranes. The 2 infants probably died from intrapartum infection, since the placentas and cords from these cases revealed microscopic evidence of infection. The infants were resuscitated after long effort, remained cyanotic, had labored respirations, and died after 13 hours. Studies failed to reveal cultural or microscopic evidences of sepsis before death or at autopsy but did show focal hemorrhages in the heart, lungs, and in the adrenal glands that indicated asphyxia. One infant had the hyaline-like membrane in the lungs at death. An ascending uterine and placental infection may have been responsible for the improper breathing that caused the fetal deaths. The other 2 sepsis deaths were caused by pneumonia. One infant died at 7 days, and the other died at 13 days. Both had 20 to 30 minutes of intratracheal resuscitation. The long period of trauma and the contamination associated with intratracheal intubation and insufflation may have contributed to the pneumonia.

Seven infants died from birth injury as evidenced by lacerations of the falx or tentorium. Intracranial hemorrhage was secondary to lacerations. Six of the 7 mothers had severe complications of pregnancy other than premature delivery. The 7 infants were in respiratory difficulty from birth, and all of them succumbed by the third day of life. The hyaline membrane was an accompanying pathological finding in four. In these 4 infants one could reasonably assume that the anoxia was due to the intracranial hemorrhage and not to the hyaline membrane.

Seven other infants who died were found at autopsy examination to have intracranial hemorrhage without lacerations of the falx or tentorium. Four of the 7 mothers had serious associated complications of pregnancy, and 2 of these were delivered by cesarean section. Four of the 7 infants required prolonged and difficult artificial resuscitation. The remaining 3 had spontaneous, vigorous respiratory activity but within 24 hours developed irregular, labored respirations with cyanotic spells. It is of interest that these 3 who were free from initial respiratory difficulty had extensive pulmonary hyaline membrane formation at autopsy. This lack of initial respiratory difficulty suggests that the hyaline membrane was not present at birth and was perhaps caused by anoxia or its treatment.

In 7 infants the pulmonary alveolar hyaline-like membrane was the single major pathological finding at autopsy examination. Five of these appeared to be normal premature infants at birth and had normal, vigorous respiratory activity immediately. Normal respiratory function was lost within 3 days after delivery. An irregular, labored type of breathing with cyanosis supervened. Again it seems that the hyaline-like membrane may be associated with respiratory failure and death from anoxia, the anoxia beginning a few hours postnatally.

In the 38 autopsy examinations there were 5 instances where a clear anatomical cause for death could not be found. For 3 infants it was necessary to use the unspecific diagnosis of prematurity and atelectasis. In 2 other infants, subpleural and focal lung hemorrhages were discovered that probably were the result of asphyxia. Respiratory activity was established only after considerable resuscitative effort in 4 infants. The clinical courses of the infants were all marked by repiratory depression, and death from anoxia ensued.

Studies of Blood Oxygen Saturation.—The capillary blood oxygen values found for the 50 premature infants and for the 10 full-term infants whose mothers received no general anesthesia are shown on the accompanying scattergraph (Fig. 1) and in Tables I and II. Each infant was placed in an incubator containing 50 to 60 per cent oxygen immediately after delivery and remained there for at least an hour.

Those premature infants who had 85 per cent oxygen saturation or more at one hour of life had a neonatal mortality rate of 4 per cent. Those below 85 per cent oxygen saturation at one hour of life suffered a 22 per cent neonatal mortality rate. The accompanying tabulation shows the distribution of infants according to birth weights.

BIRTH WEIGHT	BELOW 85 OXYGEN SATURATION	ABOVE 85 OXYGEN SATURATION
1,000 – 1,499 grams	4 (2 deaths)	0
1,500 – 1,999 grams	7 (1 death)	10
2,000 – 2,499 grams	12 (2 deaths)	17 (1 death)
	23 (5 deaths, 22%)	27 (1 death, 4%)

Autopsy examination of the 5 infants in the low oxygen saturation group revealed intracranial hemorrhage in 4, 2 of whom had the hyaline membrane in their lungs. The remaining death was caused by pneumonia at 7 days of life.

Only 4 infants who were 85 per cent oxygen saturated at one hour showed any signs of irregular breathing while in oxygen. One became cyanotic a few hours after birth, had irregular, labored respirations, and died 36 hours after delivery. Postmortem examination revealed subarachnoid and intraventricular hemorrhages, and the hyaline-like pulmonary alveolar membrane. This infant was 93 per cent oxygen saturated at one hour of life, so anoxia did not exist at that time. The intracranial hemorrhage could have later produced respiratory depression and anoxia followed by death.

Since 6 premature infants studied for oxygen saturation died neonatally, they were omitted from further consideration. The following table lists the infants by weight groups (premature and full-term) above and below 85 per cent saturation at one hour of life who lived and had no demonstrable pathology that might have produced anoxia.

SURVIVING INFANTS BY WEIGHT GROUPS, ABOVE AND BELOW 85 PER CENT OXYGEN SATURATION, AT ONE HOUR OF LIFE, WHILE IN OXYGEN*

BIRTH WEIGHT IN GRAMS	NUMBER OF INFANTS WITH PER CENT OXYGEN SATURATION LEVELS				
	85 OR ABOVE		BELOW 85		BOTH
Less than 2,500	26	(59%)	18	(41%)	44
1,000-1,499	0		2		2
1,500-1,999	10		6		16
2,000-2,499	16		10		26
2,500 or more	9	(90%)	1	(10%)	10
Totals	35		19		54

*The difference between the two major weight groups (2,500 grams or more as compared to less than 2,500 grams) in achieving a percentage oxygen saturation level of 85 or above is 31 per cent (90 per cent minus 59 per cent). Even with correction for the size of the sample this difference is statistically significant (P = 0.02–0.01). (Statistical analysis by Dr. H. J. Dodge, Department of Public Health and Preventive Medicine, University of Colorado.)

Even though the numbers of infants in the lower weight groups are small, it appears that premature infants were not able to oxygenate their blood as well as mature infants under the same environmental conditions (Figs. 1 and 2). Inspection of Tables I and II will reveal comparatively high blood oxygen saturation values at birth and at one-half hour of life. This is because the infants were breathing 50 to 60 per cent oxygen when the the blood samples were taken. Supplementary oxygen speeds the transition from rather low oxygen saturation at birth to the higher values. Nine of 10 full-term infants placed in 50 to 60 per cent oxygen after delivery under regional anesthesia were more than 85 per cent oxygen saturated at one hour of life. Twenty-six 2,000 to 2,499 gram birth

TABLE I. PREMATURE INFANTS WITH BLOOD OXYGEN SATURATION UNDER 85 PER CENT, AT ONE HOUR, WHILE RECEIVING SUPPLEMENTARY OXYGEN (23)

CASE NUMBER	WEIGHT IN GRAMS	BIRTH			30 MINUTES		ONE HOUR		FIRST BREATH	CLINICAL COURSE OF INFANT	AUTOPSY
		OXYGEN CAPACITY	OXYGEN CONTENT	PER CENT SATURATION	OXYGEN CONTENT	PER CENT SATURATION	OXYGEN CONTENT	PER CENT SATURATION			
20743	1,050	16.4					11.7	71	Immediate	Satisfactory	
19996	1,080	16.8					10.1	60	15 minutes	Death 24 hours Weak, poor, gasping, and labored respirations. Cyanosis	Intraventricular and subtentorial hemorrhage
27011	1,035	15.5					12.5	81	Immediate	Irregular breathing. Retrolental fibroplasia	
12455	1,300	17.2					13.4	78	5 minutes	Respirations spontaneous but weak, then irregular, labored with cyanosis. Death 48 hours	Subgaleal hemorrhage
16594	1,500	15.0					7.0	47	Immediate	Cried immediately. Respirations irregular and grunting in ½ hour. Death 24 hour	Subarachnoid hemorrhage. Hyaline membrane
6090	1,585	16.4	4.7	29	6.7	41	9.6	59	Immediate	Cried immediately. Retrolental fibroplasia. Satisfactory course	
20055	1,650	20.6					16.6	81	Immediate	Normal	
18083	1,700	13.6					9.8	72	Immediate	Normal	
29650	1,740	19.1					11.5	60	Immediate	Irregular respirations, 3 hours	

27160	1,950	20.2					15.2	75	Immediate	Labored and rapid breathing. Pneumonia, recovered
1766	1,990	18.0	16.2	90	11.8	66	10.5	58	3 minutes	Intratracheal resuscitation Normal course
29622	2,020	18.9					15.6	83	Immediate	Normal
6125	2,070	16.7			11.9	71	13.6	81	Immediate	Cried immediately. Normal course
30296	2,080	19.7					13.6	69	Immediate	Irregular, shallow, labored respirations for 2 hours
29660	2,090	18.8			19.6	97	12.5	67	Immediate	Normal
257748 DGH	2,416	20.2					16.0	79	Immediate	Normal
6148	*2,155*	*15.1*	*9.7*	*64*	*12.1*	*80*	*10.3*	*68*	*6 minutes*	*Irregular labored respirations. Cyanosis. Death 54 hours* — *Subarachnoid hemorrhage*
31838	2,210	14.9					8.9	60	Immediate	Normal — *Atelectasis*
7908	2,240	16.2	12.6	78	15.5	96	13.4	83	4 minutes	Normal — *Prematurity*
30960	2,250	20.8					16.3	78	Immediate	Normal — *Subtentorial hemorrhage*
31837	2,350	17.5					11.9	68	Immediate	Normal — *Hyaline membrane*
5957	*2,459*	*15.3*			*14.9*	*97*	*10.6*	*69*	*16 minutes*	*Intratracheal resuscitation 20 minutes, breathing irregular.* — *Pneumonia and multiple pleural thickening*
										Death 7 days
5933	2,424	18.7	13.0	70	7.6	41	9.9	53	4 minutes	Intratracheal resuscitation

TABLE II. PREMATURE INFANTS WITH BLOOD OXYGEN SATURATION OVER 85 PER CENT AT ONE HOUR (27)

CASE NUMBER	WEIGHT IN GRAMS	BIRTH			30 MINUTES		ONE HOUR		FIRST BREATH	CLINICAL COURSE OF INFANT	AUTOPSY
		OXYGEN CAPACITY	OXYGEN CONTENT	PER CENT SATURATION	OXYGEN CONTENT	PER CENT SATURATION	OXYGEN CONTENT	PER CENT SATURATION			
31022	1,620	19.1					16.9	89	Immediate	Cyanotic out of oxygen for 6 hours	
27053	1,690	16.4	10.7	88	9.0	74	14.3	87	Immediate	Normal	
4783	1,700	12.1					11.5	95	Immediate	Normal	
5932	1,772	17.3	14.6	84	13.2	76	16.3	94	7 minutes	Intratracheal resuscitation. Feeding problem for 8 days	
2424	1,780	15.8	8.3	53	13.2	84	14.8	94	Immediate	Normal	
29602	1,880	16.2					14.4	89	Immediate	Normal	
256804	1,912	17.3	12.9	75	16.4	95	17.0	98	Immediate	Normal	
7925	1,928	17.6	16.4	93	16.6	94	16.6	94	Immediate	Normal	
1356	1,950	16.7	6.1	37	13.2	79	15.0	90	Immediate	Shallow respirations with cyanosis out of oxygen. Normal in oxygen	
84745	1,985	18.2	14.1	78			16.7	92	Immediate	Normal	
21448	*2,000*	*18.5*					*17.3*	*94*	*Immediate*	*Spontaneous cry. Lethargic. Labored, and irregular respirations. Cyanosis. Lived 36 hours*	*Subarachnoid, and intraventricular hemorrhage. Hyaline membrane*
21453	2,020	19.2					17.6	92	Immediate	Retrolental fibroplasia	
5327 DGH	2,080	18.1	14.9	88	14.5	80	15.7	87	Immediate	Normal	
5015	2,120	17.0			15.5	91	15.8	93	Immediate	Normal	
26489	2,170	20.0					18.4	92	Immediate	Normal	
6145	2,170	13.2	14.4	77	11.7	89	12.7	96	Immediate	Normal	
3425	2,183	18.8					17.1	91	3 minutes	Irregular respirations. Normal after 12 hours.	
2478	2,240	20.2	15.4	76	17.4	86	19.3	96	4 minutes	Normal	
25200	2,300	20.5					19.1	93	Immediate	Normal	
23652	2,390	14.5					13.1	90	Immediate	Normal	
20853	2,420	18.4					15.7	85	Immediate	Normal	
25198	2,430	17.4					15.0	86	Immediate	Normal	
5913	2,450	20.0	9.8	49	12.7	64	17.7	89	Immediate	Normal	
5014	2,459	17.0	12.3	72	12.7	75	15.8	93	Immediate	Normal	
85414	2,460	16.9	7.5	44	12.9	76	15.4	91	Immediate	Normal	
6147	2,479	17.8					17.5	98	Immediate	Normal	
27187	2,495	20.3					19.0	94	Immediate	Normal	

weight infants were studied, and 39 per cent were below 85 per cent at one hour of life. Thirty-eight per cent of 16 infants in the 1,500 to 1,999 gram group were below 85 per cent oxygen saturation at one hour. Two infants who weighed less than 1,500 grams at birth and who were less than 85 per cent oxygen saturated at one hour were able to survive.
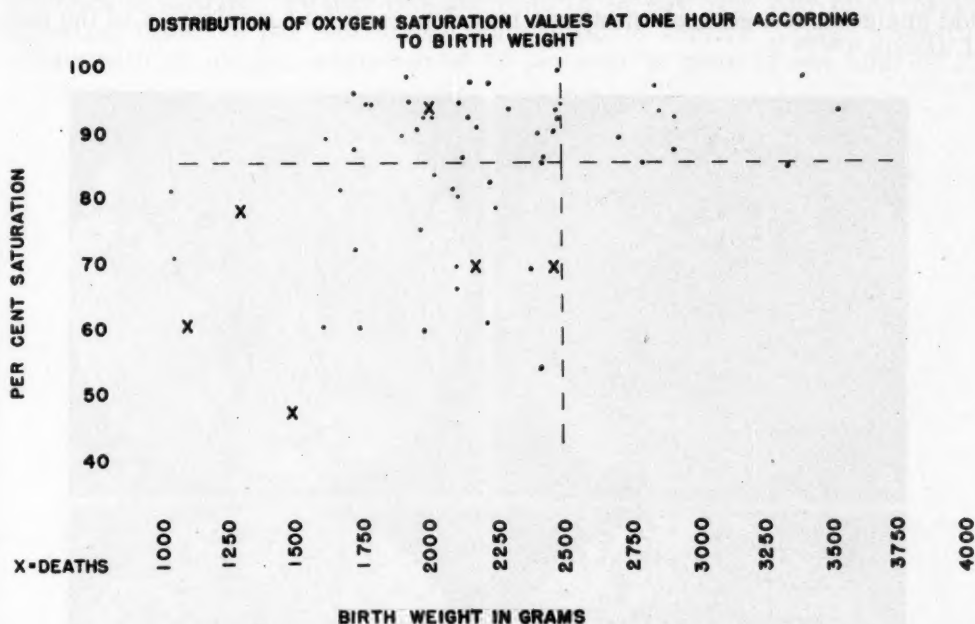
DISTRIBUTION OF OXYGEN SATURATION VALUES AT ONE HOUR ACCORDING TO BIRTH WEIGHT

X=DEATHS

BIRTH WEIGHT IN GRAMS

Fig. 1.—Each of the above 60 infants was placed in an incubator, the atmosphere of which was 50 to 60 per cent saturated with oxygen. The infants were in the incubator from soon after birth until at least one hour had passed.
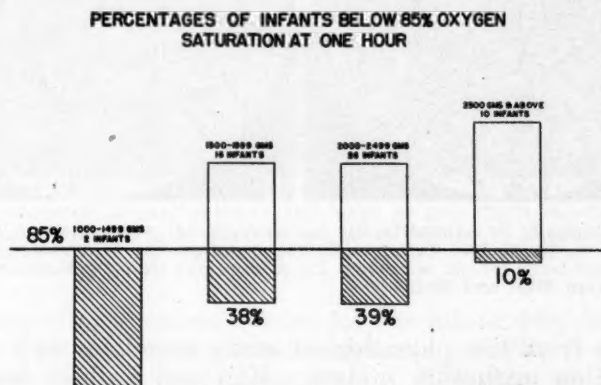
PERCENTAGES OF INFANTS BELOW 85% OXYGEN SATURATION AT ONE HOUR

Fig. 2.

Discussion

Blood Oxygen Studies.—A study of the data presented reveals that the premature infant is less able to oxygenate his blood in a 50 to 60 per cent oxygen atmosphere during the first hour of life than the full-time infant. Fig. 1 suggests that the degree of blood oxygen saturation at one hour of life may be directly proportional to birth weight. The number of premature infants in the lower weight groups, however, is insufficient for final conclusion.

The autopsy studies of premature infants and a review of the obstetrical and neonatal clinical factors surrounding each death emphasize the importance of anoxia as a cause of death among premature infants. Recognizing the anatomical basis for the immaturity of the premature infant's respiratory center and lung tissues, we have avoided the use of general anesthesia or analgesia for the relief of pain during premature labor and delivery. Others have warned that analgesia and general anesthesia may depress infant respiration to the point of anoxia.[1, 2, 14, 18]
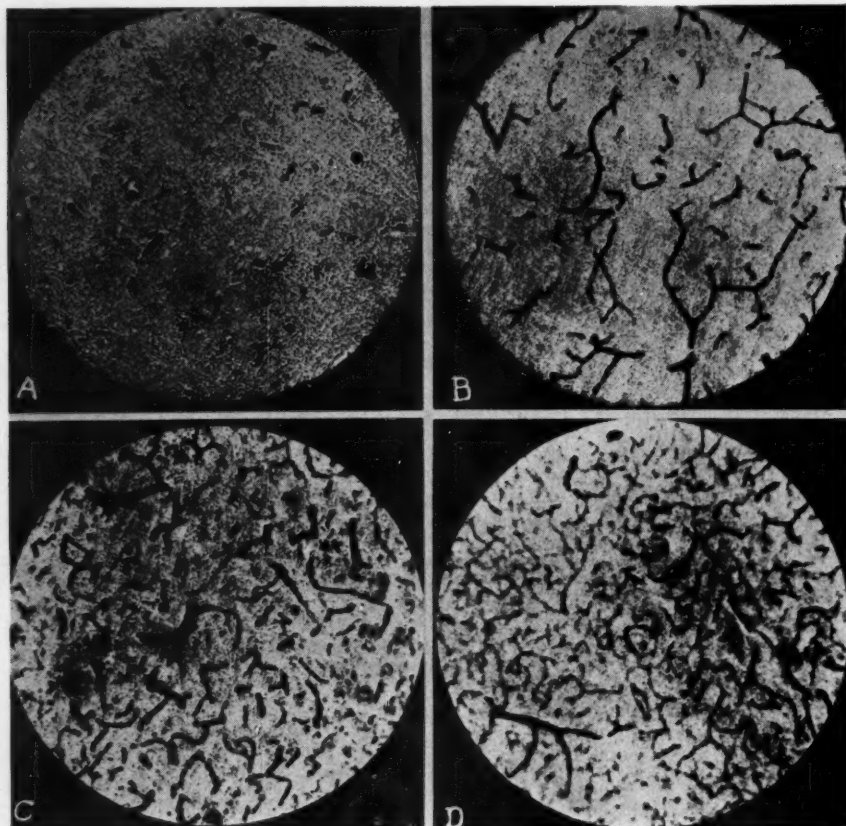

Fig. 3.—Development of capillaries in the medulla of premature infants as compared to full-term infants: A, Premature infant weighing 1 kilogram; B, Premature infant weighing 2 kilograms; C, Full-term infant weighing 2.5 kilograms; and D, Full-term infant weighing 3.4 kilograms. (From Mali and Räihä.[12])

Information from this physiological study correlates well with anatomical studies reported on premature infants. Mali and Räihä[12] demonstrated in a striking manner the progressive enrichment of the vascular supply of the medulla of infants whose weights were 1.0 kilogram, 2.0 kilograms, 2.5 kilograms, and 3.4 kilograms (Fig. 3). Klemola[8] studied the anatomical maturity of lung tissues of infants weighing 0.5 kilogram, 1.0 kilogram, 2.3 kilograms, and 3.4 kilograms (Fig. 4). The meager vascular bed in the lungs of the premature infants as compared to the more highly developed pulmonary vascular bed of the mature infant may in part explain the relatively low oxygen saturation of the blood in many premature infants after one hour of life. Fig. 5, obtained from Klemola's paper, demonstrated a similar poverty in elastic tissue in the lung of a 1.6 kilogram premature infant when compared to elastic tissue struc-

ture in a full-term infant's lung. In addition to an immature medulla and underdeveloped pulmonary structures, the premature infant often has inadequate thoracic musculature for proper respiratory function.

If, by the end of one hour of life, a premature infant does not have the blood at least 85 per cent oxygen saturated and is not breathing well in oxygen, the prognosis is serious. Twenty-two per cent (5 in 23) who had blood oxygen saturation below 85 per cent at one hour failed to survive. Those premature infants with an oxygen saturation of 85 per cent or more at one hour of life
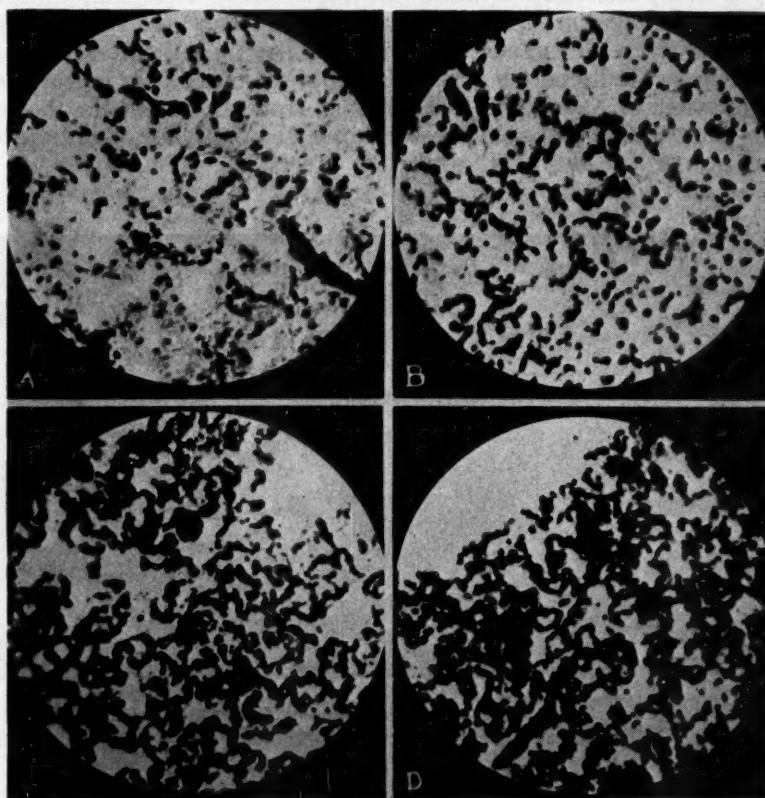

Fig. 4.—Development of capillaries in the lungs of premature infants as compared to a full-term infant: A, Premature infant weighing 0.5 kilogram; B, Premature infant weighing 1 kilogram; C, Premature infant weighing 2.3 kilograms; and D, Full-term infant weighing 3.4 kilograms. (From Klemola.[8])

had a satisfactory clinical course, except for one infant who died 36 hours after delivery. Only 4 among the 26 premature infants with 85 per cent blood oxygen saturation at one hour of life had respiratory difficulties while in oxygen.

We have not measured the effect of general anesthesia on the ability of the premature infant to oxygenate the blood during the neonatal period. Our studies on the effect of maternal general anesthesia on normal full-term infants have been reported elsewhere.[19] It was found that maternal general anesthesia, even when given in small amounts, caused some depression of blood oxygenation in normal full-term infants. It did not seem wise to repeat the same experiment on premature infants since even greater depression of infant oxygenation might be expected.

Autopsy Studies.—It is possible that deaths due to sepsis or trauma may be still further reduced. Advances in antimicrobial therapy have all but eliminated

neonatal deaths due to sepsis; we can anticipate even greater reduction in the future. Deaths due to obstetrical trauma, such as lacerations of the falx and tentorium, may possibly be reduced by wider application of existing obstetrical technique which are designed to minimize fetal depression and injury.[1, 2, 5] It is possible that caudal anesthesia may provide relaxation of the birth canal so that lacerations of the falx and tentorium will occur less frequently as the result of premature labor and delivery.

Nineteen infants (50 per cent) died from respiratory failure; intracranial hemorrhage, the pulmonary hyaline-like membrane, asphyxia, and atelectasis were found at autopsy. Further reduction of premature infant deaths from respiratory failure and intracranial hemorrhage unassociated with laceration may be made possible by better and wider application of existing obstetrical and pediatric knowledge. Prevention of deaths from these causes, however, may occur only when more is learned concerning the pathology of pregnancy, the causes for premature delivery, and the effects of prematurity on capillary fragility and on respiration.
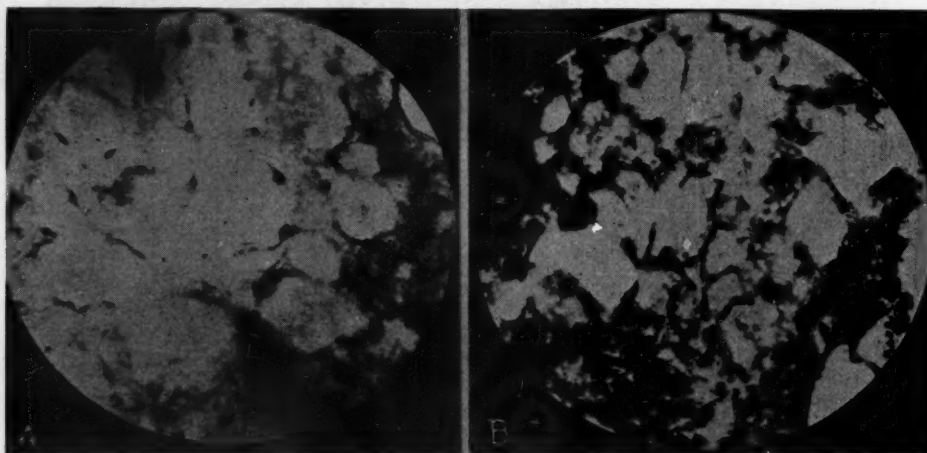

Fig. 5.—Development of elastic fibers in the lungs of a premature infant as compared to a full-term infant: A, Premature infant weighing 1.6 kilograms; B, Full-term infant weighing 3.4 kilograms. (From Klemola.[8])

Maternal Complications.—Maternal factors contributed to the death of 28 (74 per cent) of the 38 infants. Only 5 neonatal premature infant deaths (13 per cent) were associated with deliveries or labors that were uncomplicated by maternal disease or obstetrical pathology. The importance of maternal complications on premature infant survival has been previously emphasized.[20] Sixteen (42 per cent) of the 38 deaths occurred in infants where improved pediatric care could not have changed the final result. These 16 infants died of congenital anomalies, lacerations of the falx or tentorium, or failed to breathe after delivery.

The Hyaline-Like Membrane.—The hyaline-like membrane that so frequently lines the pulmonary alveolae before death of the premature infant is an interesting but not clearly understood phenomenon. Several writers have presented various theories for its formation. It seems to be acquired during extrauterine life, although Miller does not share this view entirely, since he has found the condition in four stillborn infants.[15] MacMahon[11] regards the membrane as a congenital alveolar dysplasia, while Bruns[3] has suggested that it may be a manifestation of tissue damage by excessive amounts of therapeutic oxygen. Others have thought it to be a result of aspiration.[6, 7] The hyaline membrane was found in the lungs of 18 of the 38 autopsied infants. The fact that the hyaline

membrane occurred in association with other major pathology in 12 of 18 infants is significant. In each of those 12 infants the pathology found is known to produce anoxia and death. In the remaining six, the clinical syndrome of anoxia and death developed after a few hours of normal extrauterine respiration, and the only major pathological finding was the hyaline membrane. This has led us to believe that the hyaline-like membrane is the result of anoxia, rather than the cause of the anoxia. The fundamental difficulty may be in the centers that control the mechanism of respiration. It is possible that further studies upon intracellular metabolism in the premature infant may shed light on the incomplete respiratory activity which results in anoxia and specific tissue damage. Kühn and Pichotka[9] have produced the hyaline-like membrane by subjecting animals to high concentrations of oxygen at normal or high atmospheric pressures. Bruns[3] was able to reproduce the hyaline-like membrane in guinea pigs by enclosing the animals in a high oxygen concentration atmosphere at sea level pressure.

If reduction in fetal mortality is to be obtained, deaths associated with prematurity must be reduced. One approach is the performance of careful autopsy examinations on all premature infants who die. If postmortem findings are correlated with the prenatal, natal, and neonatal experiences of the premature infant, much may be learned. An anatomic cause for death other than prematurity and atelectasis, can be found in the majority of instances.

Summary

Four and one-half years of neonatal premature infant results have been reviewed. During this period, 465 infants weighing less than 2,500 grams were born alive on the obstetrical service. The incidence of premature births was 11.7 per cent. The neonatal premature infant mortality for the same period was 13.3 per cent. Careful autopsy examinations were done on the premature infants that died. An analysis has been made of the pathological anatomical findings in infants between 1,000 and 2,500 grams. These findings have been correlated with the obstetrical histories of the mothers and the neonatal courses of the infants. Fifty per cent of the infants died from causes related to anoxia. In addition, a study has been made of the effect of prematurity on the ability of the newborn infant to oxygenate the blood during the early hours of life.

Conclusions

1. Careful performance of postmortem examinations on premature infants will reveal an anatomic cause for death in the majority of instances.

2. Measurements of the ability of premature infants to reach 85 per cent or higher blood oxygen saturation by the first hour of life reveal that premature infants are unable to perform this function as consistently as full-term infants.

3. Until more is understood concerning factors leading to premature delivery, continued emphasis should be placed on the necessity for avoiding the use of the analgesic and anesthetic agents which depress the immature respiratory centers of premature infants.

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4200 EAST NINTH AVENUE

Discussion

DR. L. M. RANDALL, Rochester, Minn.—The wastage among premature infants has been of concern for many years. While this will always be a joint problem for the obstetrician and pediatrician, each has some separate responsibility in the matter, a point well emphasized by Dr. Taylor and his colleagues.

When one attempts to evaluate the fetal causes for this wastage in the individual case, considerable difficulty arises. The results of postmortem examinations of premature infants are not always interpreted easily, for it is difficult to know how much fetal death may be charged to external factors. The tissue of the premature infant may not be developed sufficiently to withstand even minimal trauma and, therefore, may be unable to cope with the process of birth and the subsequent struggle to exist under the best of conditions. The excellent study presented here clearly demonstrates one aspect of this situation, the inability of the premature infant to attain quickly the normal oxygen saturation and the effect of this on immature tissues. The cause of the hyaline membrane seems obscure but to me further represents a part of the whole picture.

The authors found among 38 infants, 8 (21 per cent) with defects not compatible with extrauterine life and 12 (31 per cent) in whom a hyaline membrane or no apparent cause of death was found. This is a total of 52 per cent of cases in which inadequate development or developmental defects weigh heavily against salvage.

Among 1,486 infants born on our service (Mayo Clinic), 96 (6.4 per cent) were premature; of these 77 were born alive and of those weighing between 1,000 and 2,500 grams the salvage was 92 per cent, identical with results reported in this paper. For some reason, in our sample the incidence of maternal complications contributing to the premature live births was much lower than in the experience of Dr. Taylor. On the other hand, among 19 premature stillbirths the factor of maternal and obstetrical complications was very high.

Maternal conditions do contribute to the death of live premature infants. Many of these are preventable and others amenable to treatment, but there will continue to occur those conditions which may not be controlled until maturity of the infant without undue risk to mother and infant; among others spontaneous premature labor will occur for reasons that are unknown.

We have then the problem of attempting, within our present abilities, to supply the most favorable environment during pregnancy, parturition, and the neonatal period, to offset the inherent defect of prematurity. We have also the problem of improving our facilities for treatment of those conditions, maternal and fetal, responsible for wastage among prematures, realizing the great difficulty, perhaps impossibility, of being able to duplicate intrauterine conditions. No one has as yet been able to replace the function of a very important endocrine gland, the placenta.

DR. WILLIAM J. DIECKMANN, Chicago, Ill.—I wish to compliment Dr. Taylor on his very low neonatal premature mortality and on a worth-while study.

We know from postmortem examinations that many premature babies die after delivery without any obvious pathology. It is the first report, so far as I know, of serial observations on oxygen capacity and content which has been reported.

We have been making similar studies with a different technique. We deliver the umbilical cord through a small incision at the time of cesarean section under local anesthesia; obtain a sample of arterial or venous or both types of blood, then administer oxygen or an anesthetic, and obtain additional samples. We have had as long as fifteen minutes between the control and test specimen although there is no reason why one could not wait for a half-hour. The baby, of course, during this time is in utero with the normal circulation. The babies are then followed by our pediatricians with an oximeter. These studies of the physiology of the newborn baby will, I believe, explain some of the deaths without any demonstrable pathology and will enable us to save these babies.

I wish to ask Dr. Taylor whether he has made any comparisons of capillary and venous bloods in these babies. In the adult the capillary blood is similar to arterial blood. We obtained cord blood, venous blood, and capillary blood just as quickly as possible and found that the capillary blood had a much higher oxygen capacity, hematocrit, and red cell count than either the venous or cord blood. It remains higher than the venous blood even at two weeks post partum. I do not know when the values become like those found in the adult. Poncher, at the University of Illinois, has made the same observation. Windle has also made a similar observation. Our values in a number of babies were as follows:

	OXYGEN	
	CAPACITY ML.	SATURATION %
Cord vein blood, mean	16.8	31-69
Venous blood, mean	17.5	
Capillary blood, mean	22.0	

DR. WILLARD M. ALLEN, St. Louis, Mo.—Since Dr. Taylor has referred to some work by W. H. Masters in my department, it may be worth while to describe his findings. A few years ago we began using continuous caudal analgesia first on ward patients and then increasingly on private patients. In the course of the period when this analgesic agent was first being used, many more patients received general anesthesia than received continuous caudal. These premature infants went to the same nursery as the infants of mothers who had received nitrous oxide, ether, chloroform, or other forms of inhalation anesthesia. When we analyzed this series of cases we found that the salvage rate among prematures whose mothers had had caudal and nothing else was somewhat more than twice as great as in the other group who had had inhalation anesthesia.

The other point that I would like to bring up is that the incidence of prematurity that Dr. Taylor gives is higher than it is in our hospital. I wonder if he has any explanation for this high rate of prematurity?

DR. TAYLOR (Closing).—I was interested to find that at the Mayo Clinic Dr. Randall's results with premature infants parallel ours.

Dr. Dieckmann asked about a comparison of capillary blood and aerated venous blood. We have found in our experience that, although capillary blood saturation is a little higher, it is not appreciably higher than aerated venous blood from the same patient.

Dr. Allen remarked about our incidence of prematurity. You will recall that we mentioned that in our four and one-half year period the incidence of prematurity was 11.7 per cent, whereas the general incidence of prematurity in this country is around 5 to 7 per cent. As has been pointed out by others, Dr. Eastman especially, medically indigent patients tend to have a high incidence of prematurity. Whether it has anything to do with nutrition or altitude I do not know but I think it is the combination of factors that makes the indigent person less desirable from the obstetrical risk standpoint.

PAGET'S DISEASE OF THE VULVA*

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PAGET'S disease, usually occurring as a low-grade carcinoma of the breast, may develop in extramammary areas in which apocrine glands are found (axillary, genital, and perianal regions). Paget's disease of the vulva, though rare in occurrence, presents a unique clinical and pathological picture. Grossly, the vulvar lesion is a sharply demarcated, reddened, eczematoid, and ulcerated area which causes tingling, itching, and pain. Microscopically, the characteristic large ovoid or rounded Paget cells with large vesicular nuclei and pale-staining finely granular or vacuolated cytoplasm present an unusual appearance as they lie singly or in groups between the nonneoplastic epidermal cells.

In 1874, Sir James Paget[1] published the classic description of an intensely red, raw, finely granular, eczematoid, and ulcerated lesion of the nipple and areola which has since borne his name. He suggested the possibility of identical lesions involving other areas of the body. In 1937, Weiner[2] critically reviewed the literature since Paget's original article and found only 15 cases reported in sufficient detail to warrant a definite diagnosis of extramammary Paget's disease. Of these, 8 cases occurred on the vulva, 4 cases on the male genitals, and 3 cases in the axilla. Since 1937, the following have each reported a case of Paget's disease of the vulva: E. F. Traub (1943),[3] W. A. Casper (1948),[4] J. DiPrisco and J. Convit (1948),[5] and J. C. Ahumada (1950),[6] making a total of 12 reported cases.

Material

In a review of the clinical histories and microscopic sections of 50 patients with carcinoma of the vulva and 21 patients with vulvar leucoplakia and kraurosis seen at the Indiana University Medical Center since 1937, we have found 3 cases characteristic of extramammary Paget's disease.
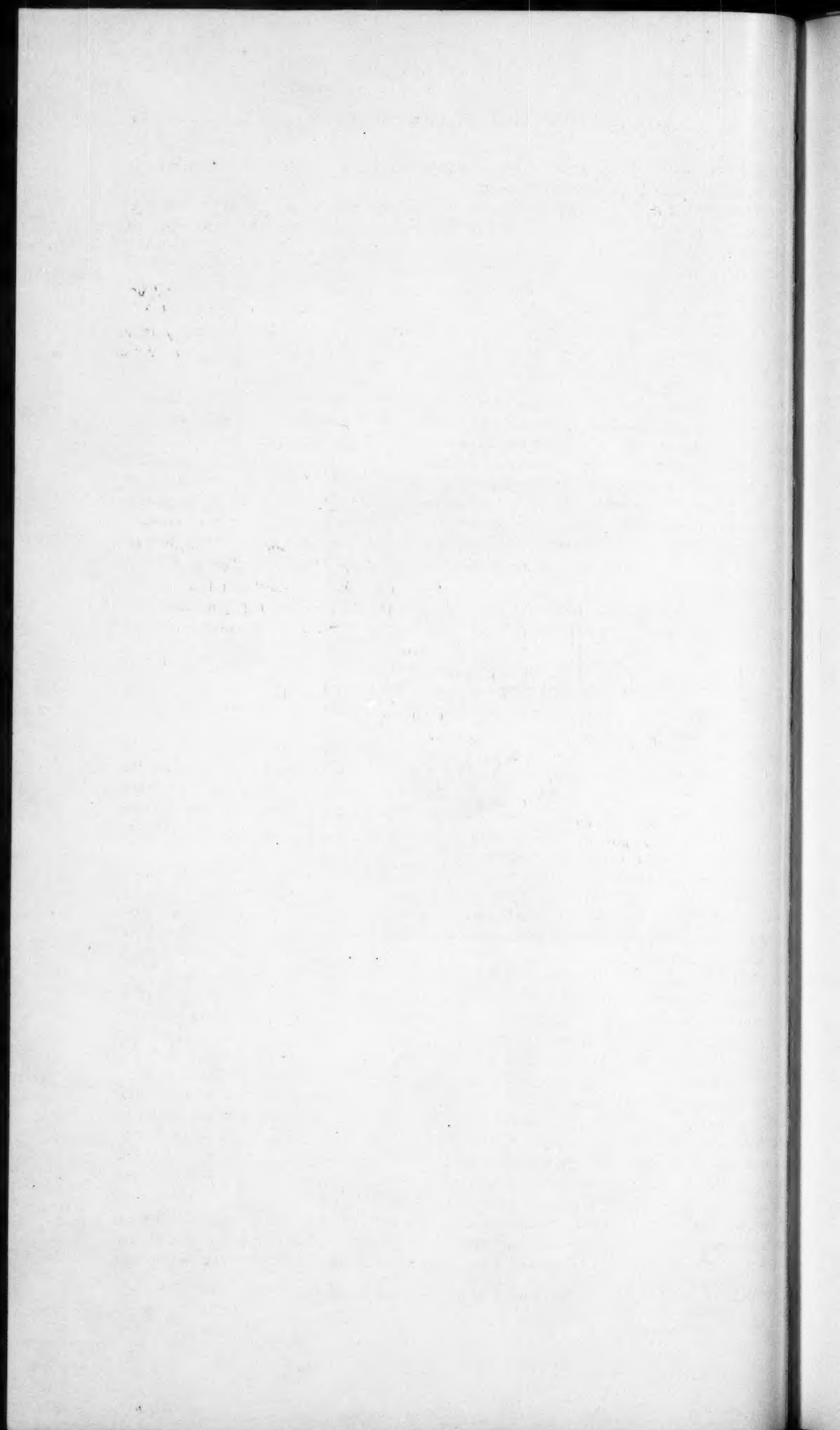
Inasmuch as there is microscopic evidence of the Paget's disease originating in a malignant transformation of apocrine gland epithelium in one of our cases and suggestive evidence of this in the other two cases, it seems pertinent to present a brief discussion of the embryologic and physiologic characteristics of the apocrine and eccrine sweat glands and the sebaceous glands. These have been very well described recently by Lever (1949).[7]

There are two types of sweat glands. The common variety is the eccrine gland which secretes without loss of cell structure. The other variety is the apocrine gland which loses a portion of its cell in the production of secretion. The mammary gland is a modified apocrine gland. Embryologically these two varieties of sweat glands are distinct. The eccrine gland according to Lever[7] is derived from the embryonal stratum germinativum and characteristically opens directly into the epidermis. The apocrine gland, like the sebaceous gland

Plate I.—Paget's disease of the vulva (Case 1).

and hair follicle, is derived from the primary epithelial germ and characteristically opens into the pilosebaceous follicle.

Apocrine glands are tubular actively secreting glands which pass through a cycle of secretory stages. The epithelial lining progresses from low cuboidal to tall columnar. Secretion takes place with loss of part of the cell cytoplasm (decapitation) into the lumen of the gland. The secretory portion of each gland has only one distinct layer of epithelial cells because the outer layer has become differentiated into myoepithelial cells. The secreting cells stain eosinophilic, in contrast to the basophilic-staining cells of the smaller eccrine glands. The sebaceous glands are holocrine glands, that is, they have no lumen, and their secretion is formed by decomposition of their cells.

CASE 1*.—Mrs. C. L. (XL 47545), aged 64 years, entered the Indiana University Medical Center, Feb. 10, 1941, complaining of itching and burning of the vulva of 17 years' duration. These symptoms began at the time of the menopause (age 46) with the appearance of a 1 cm. sized excoriated area on the vulva. During the subsequent years the area very gradually increased in size in spite of various treatments including ultraviolet light and small doses of x-ray. As the disease progressed, "little knots looking like blood blisters" would appear in the adjacent skin. These would break down, resulting in a further extension of the reddened excoriated lesion. Eventually, the entire vulva, perineum, and the left perianal area became involved (Plate I). The itching and buring became so intense that her scratching produced a secondary infection.

Past History.—She had had three normal term pregnancies. Perineorrhaphy had been performed at age 46 years; appendectomy at 54. There was no history of venereal disease or arsenical therapy.

Examination.—Inspection of the vulva revealed a reddened, eczematoid, moist lesion involving the entire vulva and extending onto the inner aspect of each thigh and the perianal tissues. There was no involvement of the mucous membranes of the vagina or anus. There were no palpable inguinal nodes.

Following a diagnostic biopsy, a radical vulvectomy was performed Feb. 5, 1941. The biopsy and the surgical specimen were examined by Dr. Clyde G. Culbertson, who made the diagnosis of Paget's carcinoma of the vulva (Path. Nos. 27,229 and 27,269). Multiple sections through these specimens show disruption of the normal pattern of the surface epithelium by atypical cells occurring singly or in groups, neoplastic changes in apocrine sweat glands, and invasion of the corium by carcinoma cells (Fig. 1).

In the surface epithelium are large ovoid or rounded cells with large vesicular nuclei and with a pale-staining, finely granular or vacuolated cytoplasm occurring singly or in groups. These cells sometimes occur between the normal basal cells. More frequently they have crowded between the polygonal cells of the stratum germinativum and into the granular layer, when the latter is demonstrable. In some areas the number of atypical cells is sufficient to effect complete disruption of the surface epithelium (Fig. 2).

In those areas where the surface epithelium is intact normal strata can be differentiated. The polygonal cells maintain their intercellular bridges and differentiate in a normal manner into flattened keratinized cells. Their shapes are frequently altered by pressure exerted by adjacent atypical cells. The atypical cells either migrate or are carried upward into the granular and keratinized layers by the growth and differentiation of the stratified epithelium. We find no evidence of these cells differentiating into keratinized squamous cells. Those located in the granular and keratinized layers show shrinkage. Their nuclei become pyknotic. The cytoplasm may remain vacuolated. Mobilized cells, principally lymphocytes, lie in the adjacent corium. The epithelium dipping downward into hair follicles frequently shows the same changes. These histological features are wholly comparable with those noted in the epithelium in that disease of the nipple known as Paget's disease.

In certain areas of the corium are seen both atypical hyperplasia of the lining epithelium of apocrine sweat glands (Fig. 3) and invasive carcinoma just underneath the epithelium and adjacent to the fat. In the glandular structures the epithelium varies from one cell in

Fig. 1 (Case 1).—Paget cells in epithelium with neoplastic changes in apocrine glands.

thickness to twenty (Fig. 3). Some of these glandular structures are imbedded in a loose connective stroma and are definitely associated with segments of apocrine glands. The lining cells vary from a cuboidal to a rounded or polygonal cell with acidophilic finely granular or vacuolated cytoplasm and with large rounded nuclei showing considerable variation in staining reaction. The nuclei are usually vesicular. Furthermore, we are able to demonstrate that some of these cells facing the existing lumen are producing a secretion in the manner of apocrine gland epithelium (Fig. 4). These features, we consider, are indicative of malignant transformation of apocrine gland epithelium. Cells with similar morphology occur in irregular masses or in columns just underneath the involved epithelium and also deep in the dermis. In some instances these are arranged about spaces (Fig. 5).

Fig. 2 (Case 1).—Pagetized surface epithelium.

The vulvectomy healed slowly and several areas required skin grafts. The patient was readmitted April 20, 1941, because of intermittent vaginal bleeding. The vulva was well healed without evidence of recurrence. Biopsy of the cervix revealed squamous-cell carcinoma, Grade 2 (Fig. 6). She received irradiation therapy for the cervical neoplasm and died at home Feb. 20, 1942, of generalized carcinomatosis. Autopsy was not obtained. There had been no recurrence of the local vulvar lesion.

CASE 2.—Mrs. N. R. (XL 103761), aged 74 years, was admitted to the Indiana University Medical Center Oct. 25, 1946, with a chief complaint of vulvar pruritus for many years, increasing during the past three years.

Past History.—She had had two normal full-term pregnancies. Hysterectomy and appendectomy had been performed at age 49 years. There was no other pertinent history. Serologic tests for syphilis were negative.

Examination.—Inspection of vulva revealed a sharply demarcated, reddened, eczematoid lesion with superficial ulceration involving the vulva and extending posteriorly on either side of the anal orifice. The mucous membranes were not involved. There were no palpable inguinal glands.
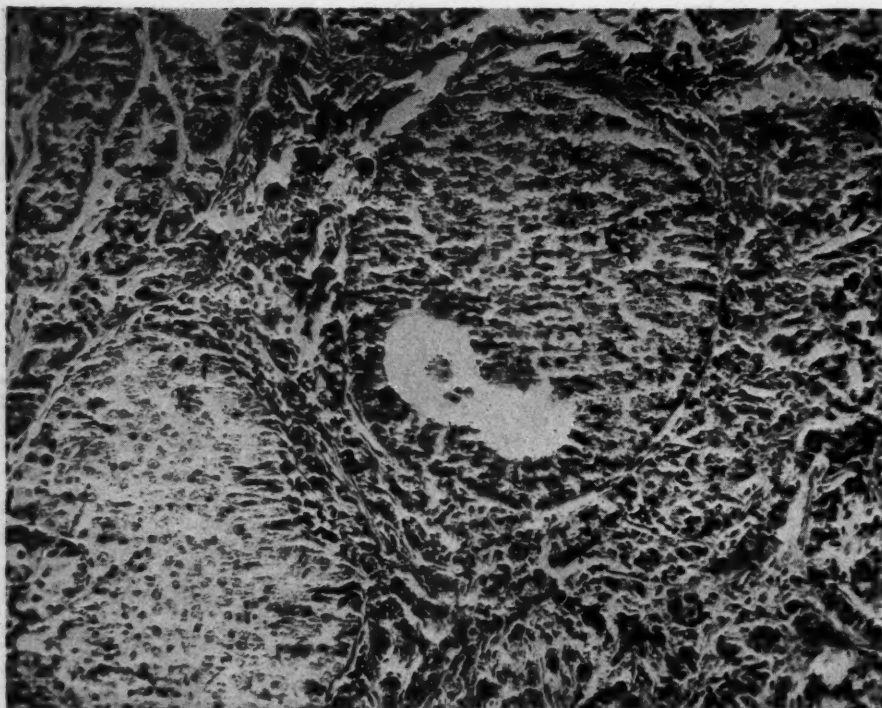
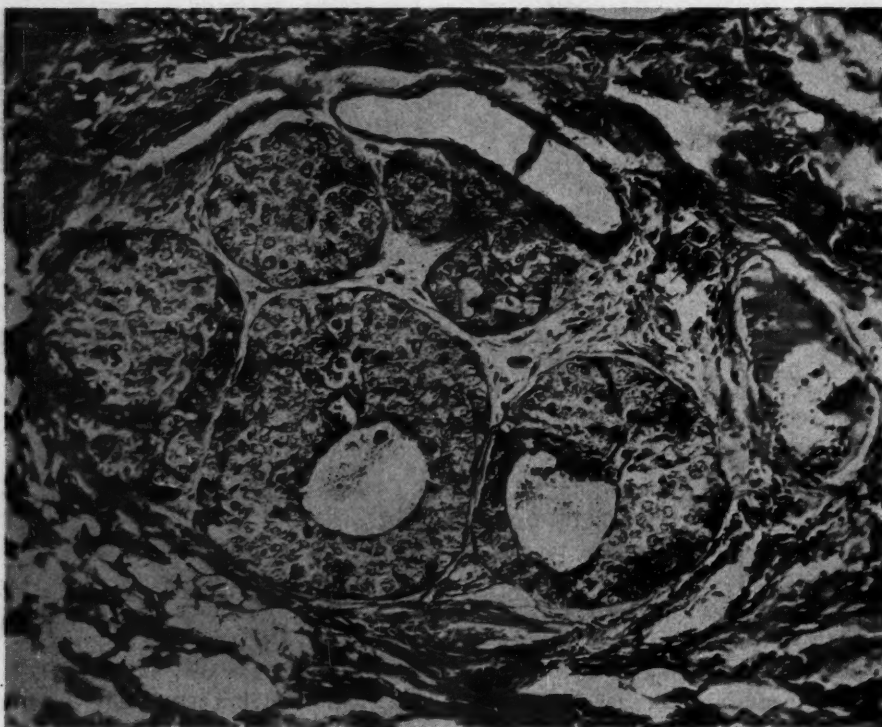Fig. 3 (Case 1).—Neoplastic apocrine gland.

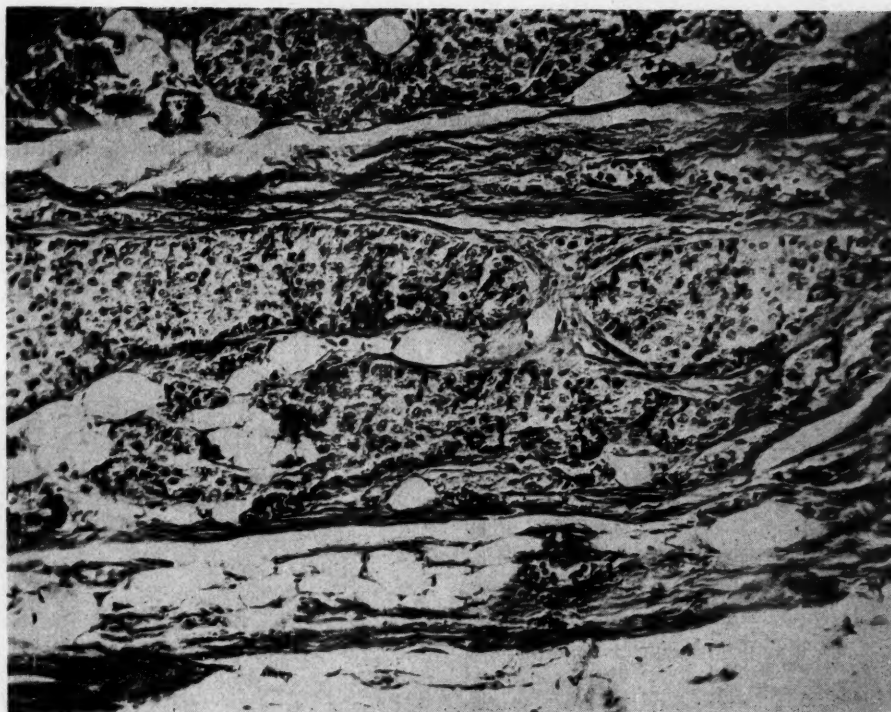Fig. 4 (Case 1).—Decapitation secretion in malignant gland.

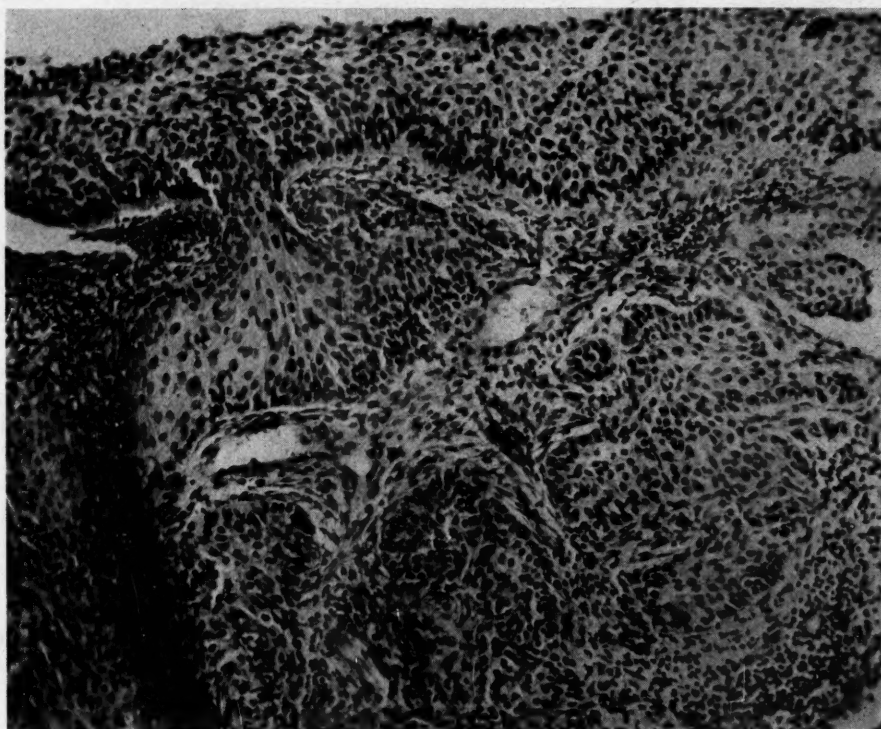Fig. 5 (Case 1).—Infiltration of neoplasm deep in dermis.

Fig. 6 (Case 1).—Squamous-cell carcinoma of cervix.

Extensive vulvectomy was performed March 1, 1946.

The tissue sections (Path. No. 44366) were read originally by Dr. J. L. Arbogast, who recognized a marked similarity to the changes recorded for the disease commonly referred to as Paget's disease. The surface epithelium again showed the presence of large rounded or ovoid cells with large vesicular nuclei and a finely granular or finely vacuolated eosinophilic cytoplasm (Fig. 7). These occurred singly or in groups. Mitoses were frequent. In this preparation some of the cells closely simulated the cells with perinuclear vacuoles noted in Bowen's disease. However, the stratified squamous epithelial cells showed normal stratification. The polygonal cells possessed well-defined intercellular bridges and retained their normal orientation except in these areas where the atypical cells had exerted undue pressure.
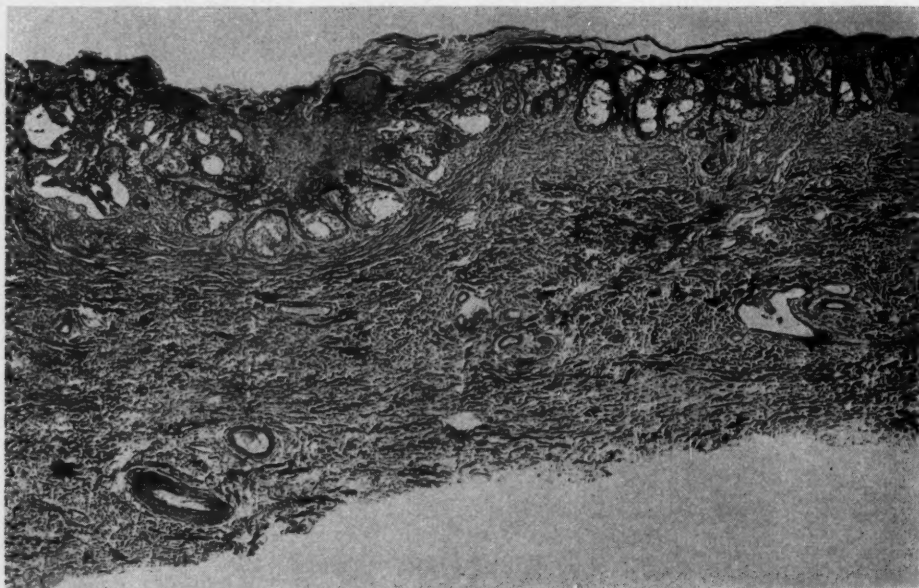

Fig. 7 (Case 2).—Paget cells in epithelium.

In a few small areas the atypical epithelium was arranged about spaces (Fig. 8). Such formations lie in contact with the basal portion of the surface epithelium. Usually the epithelium about such spaces is multilayered, but it is possible to demonstrate single-layered epithelium occasionally. In the available material we have not demonstrated any features to suggest production of secretion nor have we demonstrated invasion of the corium. In some areas the surface epithelium is so disrupted that sloughing has occurred (Fig. 9). Our findings are those of intraepithelial invasion by carcinoma simulating closely the intraepithelial involvement in the disease commonly known as Paget's disease.

The patient did not return following discharge from the hospital. The vulvectomy wound had healed satisfactorily. Follow-up investigation revealed that the patient died in a nursing home Nov. 10, 1949. The death certificate listed generalized carcinomatosis of 6 months' duration, origin undetermined, as the cause of death.

CASE 3.—Mrs. L. H. (XL 116839), aged 68 years, was admitted to the Indiana University Medical Center Feb. 12, 1948, with a history of vulvar and perianal pruritus for 8 years. She had received local x-ray therapy without relief one and one-half years prior to admission.

Past History.—She had hypertensive heart disease of some years' duration. Cholecystectomy had been performed in 1939. Serologic test for syphilis was negative.
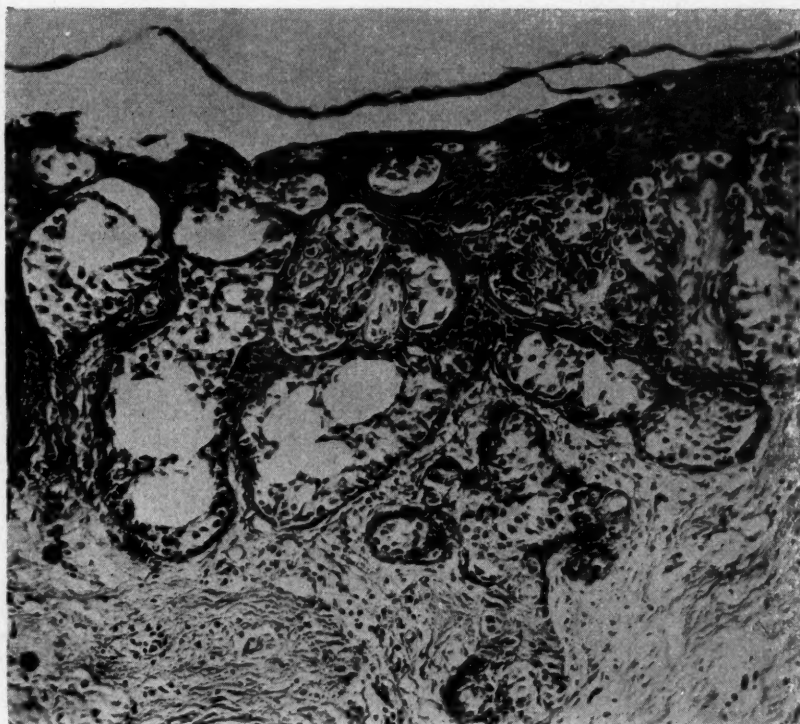
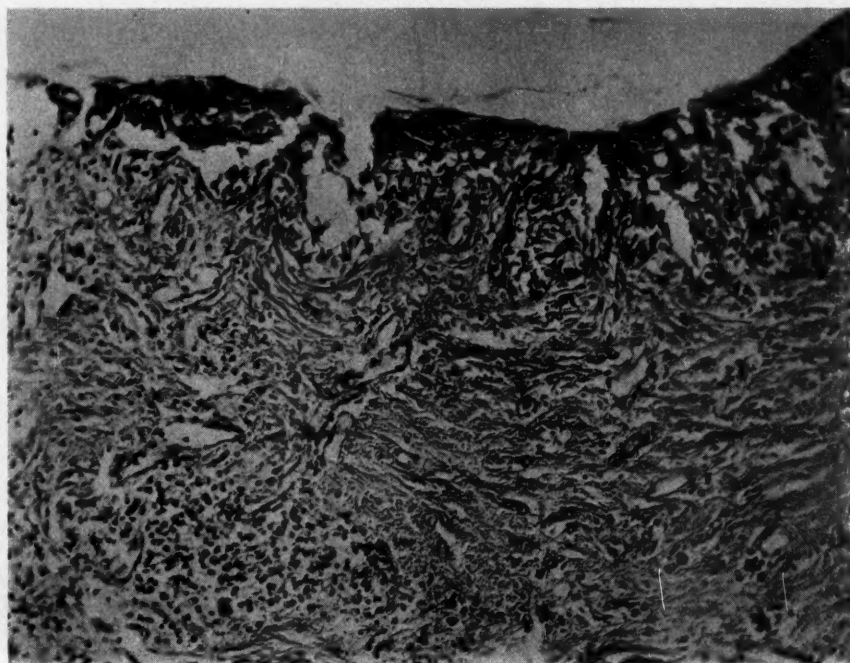Fig. 8 (Case 2).—Adenomatous pattern in contact with basal portion of epithelium.

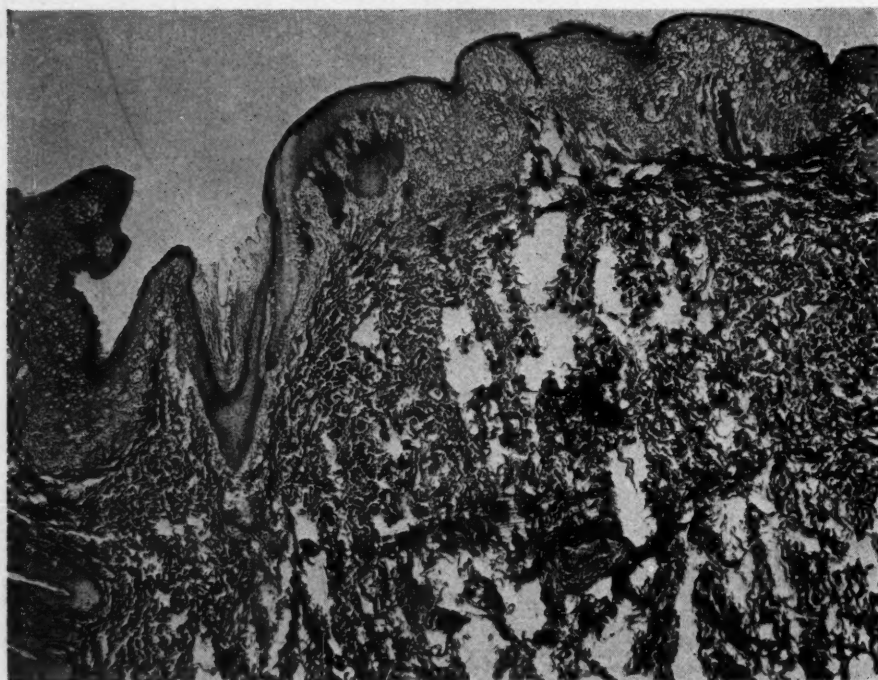Fig. 9 (Case 2).—Disruption of surface epithelium with sloughing.

Fig. 10 (Case 3).—Paget cells in stratified squamous epithelium.

Fig. 11 (Case 3).—Preservation of intercellular bridges and normal stratification of epithelium.

Examination.—There was a raised, whitish, eroded lesion involving the vulva and extending onto the skin of the inner aspect of the left thigh. There were no palpable inguinal lymph nodes, and there was no extension to the mucous membranes.

On Feb. 23, 1948, a simple vulvectomy removing the involved skin surface was performed. The dissection was limited because the patient was a poor operative risk due to her cardiac status.

On microscopic examination (Path. No. 48531), the intraepithelial changes in the areas examined showed the same Paget cells in the stratified squamous epithelium as were demonstrated in the two previous cases (Fig. 10). This photomicrograph shows large rounded cells with vesicular nuclei and with finely vacuolated cytoplasm occurring singly and in groups in various layers of a hyperkeratotic stratified squamous epithelium (Figs. 11 and 12).

Fig. 12 (Case 3).—Mitosis in vacuolated Paget cells.

In one area the surface epithelium had grown over a thin layer of granulation tissue. Here the surface epithelium was hyperkeratotic and extended downward into the granulation tissue and also into apocrine gland elements. This epithelium was well differentiated. We believe this to be vigorously growing and well-differentiated epithelium at the site of an erosion rather than a neopalstic change.

Examination 20 months later revealed no recurrence of vulvar pruritus or local lesion. Recent report indicates that the patient is alive but unable to return for examination due to her cardiac disease.

Comment

The gross and microscopic characteristics of these 3 cases are identical with those seen in Paget's disease of the nipple (Fig. 13). There is general agreement regarding the clinical and microscopic interpretation of Paget's disease of the nipple as being a low-grade carcinoma. However, there have been many disagreements concerning the diagnosis of extramammary Paget's disease of the vulva.[2, 8, 9, 10, 11]

The most frequent difference of opinion is concerning the diagnoses of Paget's disease and Bowen's disease. Grossly and symptomatically the two

lesions are not alike. Paget[1] in his original publication described a lesion which was a "florid, intensely red, raw surface, very finely granular, as if nearly the whole thickness of the epidermis were removed; like the surface of a very diffuse eczema. . . . The sensations were commonly tingling, itching and burning." Bowen[12] in characterizing the lesions which bear his name described a chronic affection of the skin which may "attack any portion of the integument and begins as a papule, pale red, or the color of normal skin. This papule is covered by a thick layer which may be excessive and usually is combined with serous exudation to form a cornified crust. These papules increase to form lenticular or rounded, nodular lesions which may remain discrete or often tend to be grouped or confluent. When the crust is removed the surface beneath is found to be red and oozing, granular and sometimes slightly papillomatous in appearance." The subjective symptoms of these lesions were slight. Bowen stated that the lesions he had described were distinctly different from any previously described skin disease, including extramammary Paget's disease.

Fig. 13.—Paget's disease of nipple.

Microscopically the epidermis in Paget's disease shows acanthosis but otherwise shows little change in its character. The large, clear Paget's cells devoid of prickles are scattered through the epidermis. Their nuclei are large, round, and pale staining, and are usually in the basal layer. They may be so numerous that the normal cells are compressed and form only a network filled with Paget cells. In Bowen's disease as well as arsenical keratosis large vacuolated epidermal cells may be found but in contrast to Paget cells they possess prickles. Characteristically in Bowen's disease one finds clumping of the nuclei within (Fig. 14) multinucleated epithelial giant cells and also individual cell keratinization which is not present in Paget's disease. Erythroplasia of Queyrat is like Bowen's disease of the mucosa and progresses rapidly into squamous-cell carcinoma.[7] The carcinoma associated with Paget's disease is an adenocarcinoma arising in the apocrine glands and is entirely different. No other form of carcinoma of the apocrine glands has been established.[7] Hidradenoma is a benign adenoma of these glands (Novak).[13]

Fig. 14.—Bowen's disease of skin.

Conclusions

1. The lesion which we have described and illustrated is grossly characterized by a slowly spreading eczematoid change in the skin identical with that seen in Paget's disease of the nipple.

2. The carcinomatous character of the lesion with underlying adenocarcinoma of the apocrine glands (Case 1) mandates careful microscopic study of suspected tissue.

3. The fact that extramammary Paget's disease is always found in skin areas in which apocrine glands are characteristically present strongly suggests that the lesion is identical in nature with Paget's disease of the nipple.

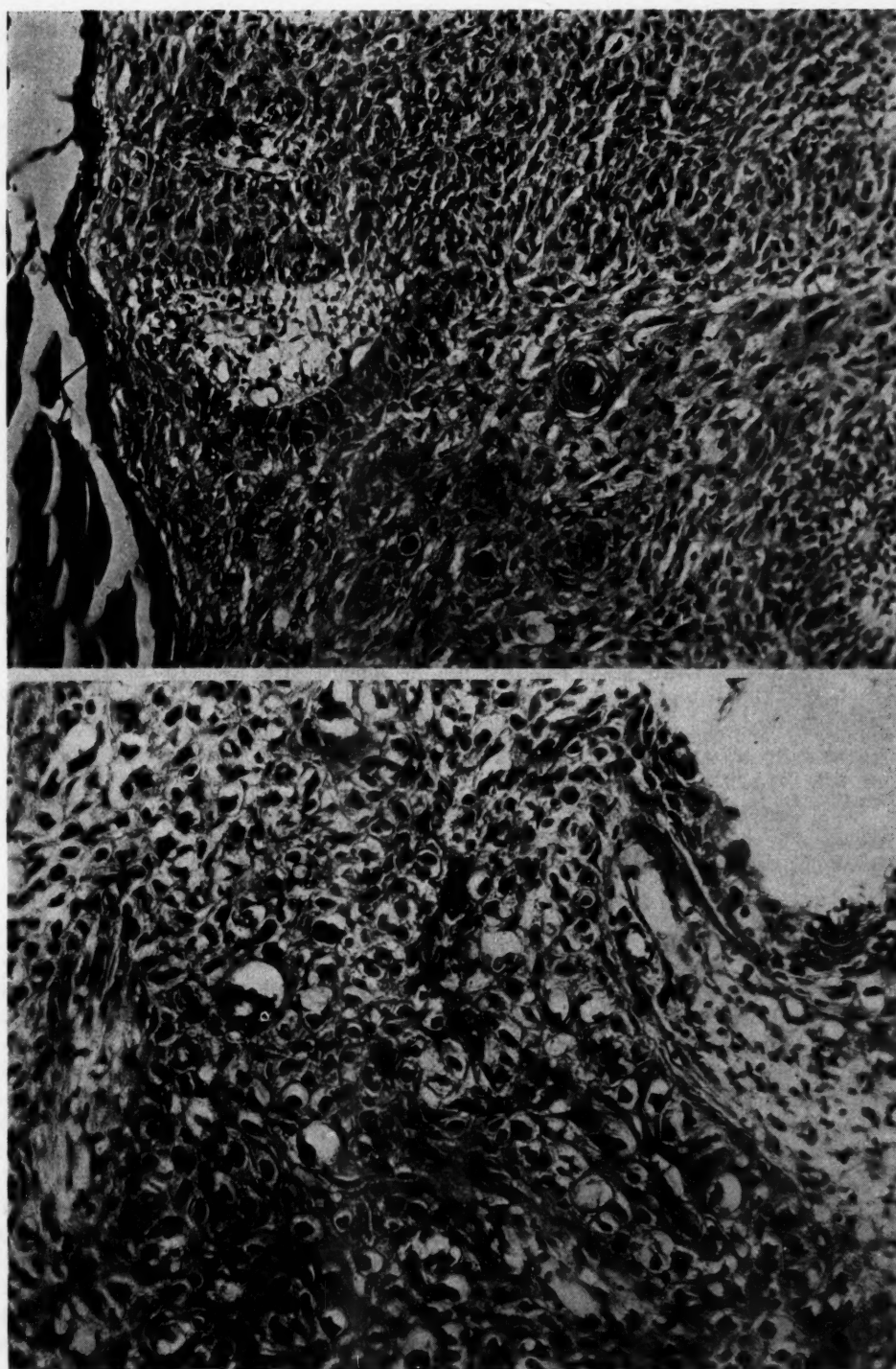4. Treatment should be that of wide and deep excision with careful follow-up in spite of the long interval that has usually elapsed before definitive treatment has been employed.

5. We have presented 3 new cases of extramammary Paget's disease of the vulva. One of these shows a definite adenocarcinoma of the underlying apocrine sweat glands.

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Discussion

DR. EMIL NOVAK, Baltimore, Md.—I have no doubt that the vulvar lesion which has been so well described by Dr. Huber is a new one to most of those present, even to many of those interested in gynecologic pathology. The authors, therefore, have made a real contribution in bringing it to our attention, in spite of its rarity. It is quite clear that there are still many controversial points as to its real nature and its histogenesis, just as there are concerning the better known Paget's disease of the nipple. Much of this discussion revolves about the large, clear, so-called Paget cells, which are so distinctive of both the mammary and extramammary forms of the disease.

The authors are obviously impressed with the concept that the apocrine glands are the source of origin of this lesion. Their Case 1 presents better evidence in favor of this view than most others which have been reported, though it cannot be considered unimpeachable. In this case the epidermal lesion is associated with a definite lesion in the corium which certainly appears to be of apocrine gland origin. One might, therefore, suspect that the Paget cells in the epidermis represent a peculiar type of metastatic infiltration, just as some believe that the similar cells in Paget's disease of the nipple represent epidermal infiltration of a primary intraductal carcinoma. As against this view, however, a group of cases has been observed in which the epidermal lesion and the Paget cells are perfectly typical and without the slightest involvement of the corium. One would, therefore, have to assume a

widespread multicentric malignant process entirely limited to the epidermis. This view has indeed been suggested by some, but it seems to me to be highly improbable. In cases of this group it would seem more rational to believe that the Paget cells develop in the epidermis, that they are to be looked upon as precancerous rather than cancerous, and perhaps even that they may represent unripe or progenitor cells, embryologically closely related to the apocrine gland epithelium and that of the sebaceous glands. Instances of heterotopia of this type may be seen in various tissues; for example, I have seen typical sebaceous glands in the stratified squamous epithelium of the cervix. This is just another hypothesis which may be added to a good many which have been suggested to explain these peculiar cells. An embryologic concept would at least link up the two varieties of Paget's disease which various authors, like Ewing, have distinguished, one in which an underlying tumor is present and one in which it is not.

In the past few days, since Dr. Huber so kindly sent me a copy of his paper and microscopic sections from his cases, I have discussed this subject with one or two dermatologist confrères. From their comments, as well as from a review of a few articles on the subject written by dermatologists, I have been impressed with the intricacies and the confusion existing as to certain lesions of the skin and its appendages, such as sebaceous adenoma or carcinoma, apocrine adenoma and carcinoma, and a whole variety of other lesions believed to arise from the sweat glands, eccrine or apocrine. Of these, the one most familiar to gynecologists is the hidradenoma, which many believe is always of apocrine origin, although I do not think that this can be considered as established beyond doubt, for reasons which were discussed in a paper of Stevenson and myself in 1946.

I drag this lesion into this discussion because it so often exhibits a double layer of epithelium, the outer of the so-called myoepithelial type, and this is not seen in the lesions pictured in the authors' Case 1 or, so far as I know, in any of the previously described cases.

This paper emphasizes that we must add Paget's disease to the group of so-called precancerous lesions which may be encountered by the gynecologist and which includes also Bowen's disease and intraepithelial carcinoma. The latter two must be distinguished, although in the early days of our discussions of cervical carcinoma in situ they were often used interchangeably. By the same token, there are clear differences between Paget's disease and Bowen's disease, as the authors have emphasized in their paper. The microscope must usually make the distinction rather than the clinical appearance of the lesion. In talking to a dermatologist the other day, I was told simply that Paget's disease is much redder and not as "bumpy" as Bowen's disease.

DR. KARL MARTZLOFF, Portland, Ore.—This paper is so interesting that I would like to have heard a more general discussion. The one thing that impresses me in the discussion of Paget's disease as against Bowen's disease of the female nipple or the vulva is that Paget's disease does not present the customary picture which we associate with noninvasive carcinomatoid lesions. The cases reported by Dr. Huber illustrate beautifully the unusual and striking Paget cells, about which there has been so much speculation. These may lie as Dr. Huber's slides show isolated and discretely distributed among the apparently unaltered surrounding cells of the epidermis and apocrine glands, particularly at the periphery of the lesion. This is in startling contrast to the more or less general and diffusely altered epidermal cytology which occurs in areas of noninvasive carcinomatoid change or cancer in situ. The difference in cytology of these two lesions is so profound that I would like to ask Dr. Huber whether there have been any studies made to show a viral etiology for Paget's disease?

DR. HUBER (Closing).—I feel from studying these slides that there is a definite difference not only microscopically but also grossly, as Dr. Martzloff pointed out, between Paget's disease of the vulva and what is described as Bowen's disease or intraepithelial carcinoma of the vulva. The sections show a well-differentiated epidermis through which one traces all the normal stratifications and in which one can see the intracellular bridges. This epidermis invaded by large vacuolated Paget cells is entirely different in appearance from the intraepithelial carcinoma in which one finds a complete loss of stratification. Occasional

large vacuolated cells may be present but those are mixed with epidermal cells showing varying degrees of individual cell keratinization and bizarre patterns. I believe that we have not appreciated the difference because we have not had the opportunity of seeing many vulvar lesions that fit a picture like Paget's disease of the nipple. We were very fortunate to have a pathologist associated with us who described this initial case as resembling so typically mammary Paget's disease that much more complete investigation was undertaken.

I would like to emphasize a point in relation to one of the statements Dr. Novak made. He agreed that in the first case there is unquestioned carcinoma involving the apocrine sweat glands. This area was the only one in which we could demonstrate these glands. The surface epidermis shows large Paget cells present throughout many sections but apparently unrelated to underlying apocrine glands.

It is entirely possible that we do not prove the apocrine gland origin of such neoplastic changes because we do not happen to find the carcinoma in the apocrine gland that may have been the site of origin.

I wish I could answer Dr. Martzloff's question about virus etiology. I do not think there is any evidence that would support the idea that Paget's disease of the nipple or that extramammary Paget's disease is a virus disease.

A BACTERIOLOGIC AND CLINICAL STUDY OF PYOMETRA*

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A T THE sixty-seventh meeting of this Society in 1942, a paper[1] on the bacteriologic findings in pyometra was presented. In that paper an effort was made to review the literature on pyometra and to indicate the pathologic conditions which antedated the formation of true pyometra.

In the consideration of the importance of infection in the predisposing pathologic conditions which precede the formation of pyometra, emphasis was placed on the scarcity of reports on the bacteriologic studies in pyometra.

With the increasing knowledge of the part that anaerobic organisms played in pelvic infections, it was obvious that any bacteriologic attempt to study pyometra must include the study of complete anaerobic cultures as well as the more readily studied aerobic cultures. It was emphasized that the study of the various anaerobic organisms was difficult and the grouping of these organisms was unsatisfactory. It was also obvious that much detailed bacteriologic work on these anaerobic organisms was necessary before the misunderstandings and the confusion in their classification could be corrected.

Since 1942 we have continued the study of the bacteriologic problems of pyometra. In the interval no paper on the bacteriology of pyometra has been found in the literature.

Melody[2] has presented the salient features of the obstructed cervix. DeVoe and Randall[3] have given an excellent clinical and pathologic study of pyometra.

Material

This is a report on 133 patients who had pyometra. These 133 patients do not in any way represent the true incidence of pyometra in our clinic. Many other patients had evacuation of pyometra by our routine practice of sounding all endocervical canals as a necessary part of all gynecologic examinations. Many of these patients with pyometra could not be included in this report because of the failure to obtain properly the pus for culture. Possible contamination from the vagina and the inability to expedite the planting of the anaerobic cultures under properly controlled conditions were considered proper reasons for the exclusion of these patients from this series.

Pyometra is more common than a review of the literature suggests. The incidence will increase with any sensible and well-controlled plan to ensure patency of the endocervical canal.

Usually efforts to maintain patency of the endocervical canal are good in those patients who give histories of any types of operations on the cervices and

TABLE I. PYOMETRA COMPLICATING MALIGNANCY (SQUAMOUS-CELL CARCINOMA OF CERVIX)

PREVIOUS THERAPY	NO. OF PATIENTS	AGE (YR.)	RACE		PARITY		MARITAL STATUS			SYMPTOMS				STAGES OF CARCINOMA				C.C. PUS	PREVIOUS HORMONES
			WHITE	NEGRO	NULLIPARAS	MULTIPARAS	MARRIED	WIDOWED	SINGLE	BLEEDING	DISCHARGE	PAIN	FEVER	1-2	2-3	3-4	4-5		
None	22	50 to 69	16	6	2	20	18	4	0	22	22	8	7	20	2	0	0	5 to 150	None
Radium	2	28 and 45	2	0	0	2	2	0	0	1	1	1	0	2	0	0	0	8 and 5	None
X-ray	20	26 to 80	10	10	0	20	17	3	0	14	14	12	11	8	3	8	1	4 to 150	None
X-ray and radium	25	30 to 70	17	8	0	25	22	3	0	11	11	16	8	11	11	3	0	5 to 300	None
Totals	69	-	45	24	2	67	59	10	0	48	48	37	26	41	16	11	1	-	None

TABLE II. PYOMETRA COMPLICATING MALIGNANCY (ADENOCARCINOMA OF THE CERVIX)

PREVIOUS THERAPY	NO. OF PATIENTS	AGE (YR.)	RACE		PARITY		MARITAL STATUS			SYMPTOMS				STAGES OF CARCINOMA				C.C. PUS	PREVIOUS HORMONES
			WHITE	NEGRO	NULLIPARAS	MULTIPARAS	MARRIED	WIDOWED	SINGLE	BLEEDING	DISCHARGE	PAIN	FEVER	1-2	2-3	3-4	4-5		
None	2	49 58	1	1	0	2	1	1	0	2	2	0	0	2	0	0	0	10 and 15	None
X-ray	2	38 42	1	1	1	1	2	0	0	2	2	2	2	1	1	0	0	10 and 50	None
X-ray and radium	2	69 77	1	1	0	2	1	1	0	2	2	1	1	0	2	0	0	20 and 50	None
Totals	6	-	3	3	1	5	4	2	0	6	6	3	3	3	3	0	0	-	None

also in those patients who have been, or who are being, treated by irradiation therapy for malignant neoplasms. These efforts to maintain patency of the endocervical canal are not good in that great group of postmenopausal patients in which "spontaneous" pyometra is so often discovered in association with the postmenopausal atrophies and stenoses of the cervix.

It should be stated that with this policy of stressing the importance of maintaining endocervical patency, no uterus or cervical stump has been removed by vaginal or by abdominal operation in which pyometra has been found.

Clinical Data

Tables I to V show our clinical groupings of the 133 patients and give the clinical data for each grouping.

TABLE III. PYOMETRA COMPLICATING MALIGNANCY (ADENOCARCINOMA OF THE ENDOMETRIUM)

PREVIOUS THERAPY	NO. OF PATIENTS	AGE (YR.)	RACE		PARITY		MARITAL STATUS			SYMPTOMS				C.C. PUS	PREVIOUS HORMONES
			WHITE	NEGRO	NULLIPARAS	MULTIPARAS	MARRIED	WIDOWED	SINGLE	BLEEDING	DISCHARGE	PAIN	FEVER		
None	12	52 to 80	8	4	2	10	11	0	1	12	5	0	4	10 to 500	None
Radium	2	56 and 64	2	0	0	2	1	1	0	2	0	2	1	20 and 100	None
X-ray	2	59 and 65	1	1	0	2	2	0	0	1	1	1	0	50 and 60	None
X-ray and radium	1	70	1	0	0	1	1	0	0	1	0	0	0	15	None
Totals	17	–	12	5	2	15	15	1	1	16	6	3	5	–	None

The first four tables give the data for the 95 patients who had malignant neoplasms. Table I gives the data for 69 patients with squamous-cell carcinoma of the cervix; Table II gives the data for 6 patients with adenocarcinoma of the cervix; Table III gives the data for 17 patients with adenocarcinoma of the endometrium; Table IV gives the data for 2 patients with adenoacanthoma, and for one patient with sarcoma of the endometrium.

TABLE IV. PYOMETRA COMPLICATING MALIGNANCY (ADENOACANTHOMA)

PREVIOUS THERAPY	NO. OF PATIENTS	AGE (YR.)	RACE		PARITY		MARITAL STATUS			SYMPTOMS				C.C. PUS	PREVIOUS HORMONES
			WHITE	NEGRO	NULLIPARAS	MULTIPARAS	MARRIED	WIDOWED	SINGLE	BLEEDING	DISCHARGE	PAIN	FEVER		
None	2	77 and 55	0	2	0	2	0	2	0	2	0	1	0	50 and 200	None
SARCOMA															
None	1	46	0	1	0	1	1	0	0	1	1	1	0	30	None

Table V gives the data for 38 patients with pyometra not associated with malignancy.

TABLE V. PYOMETRA ASSOCIATED WITH OTHER CONDITIONS (STENOSIS OF CERVIX, 29 PATIENTS POSTMENOPAUSAL)

PREVIOUS THERAPY	NO. OF PATIENTS	AGE (YR.)	RACE		PARITY		MARITAL STATUS			SYMPTOMS				C.C. PUS	PREVIOUS HORMONES
			WHITE	NEGRO	NULLIPARAS	MULTIPARAS	MARRIED	WIDOWED	SINGLE	BLEEDING	DISCHARGE	PAIN	FEVER		
None	30	42 to 74	18	12	4	26	22	8	0	24	13	9	8	5 to 100	1
OPERATIONS ON CERVIX (CAUTERIZATION)															
Cauterization	4	39 44 56 64	4	0	0	4	4	0	0	2	2	2	0	25 15 10 8	0
TUBERCULOSIS OF ENDOMETRIUM															
None	2	52 64	1	1	0	2	1	1	0	2	2	2	2	80 160	0
COLLECTION OF PUS IN CERVICAL STUMP															
Supravaginal hysterectomy	1	30	1	0	0	1	1	0	0	0	1	0	0	50	0
Same plus radium 1 yr. ago	1	39	1	0	0	1	1	0	0	1	1	1	1	8	1

Tables VI to VIII give the therapy and the culture results in pyometra in 69 patients with squamous-cell carcinoma of the cervix; in 6 patients with adenocarcinoma of the cervix; in 2 patients with adenoacanthoma; in one patient with sarcoma of the endometrium; in 17 patients with adenocarcinoma of the endometrium.

TABLE VI. PYOMETRA (SQUAMOUS-CELL CARCINOMA OF CERVIX)

PREVIOUS THERAPY	NUMBER PATIENTS	CULTURES			
		NEGATIVE	ANAEROBIC BACTERIA	AEROBIC BACTERIA	MIXED ANAEROBIC AND AEROBIC BACTERIA
None	22	6	6	3	7
Radium	2	0	0	1	1
X-ray	20	2	7	1	10
X-ray and radium	25	3	8	0	14
Totals	69	11	21	5	32

Table IX gives the data on 38 patients who did not have malignant neoplasms. Thirty patients, 29 of whom were postmenopausal, had stenosis of the cervix for which no operative procedures were responsible. Four patients, two of whom were postmenopausal, had stenosis of the cervix which was thought to have been caused by previous cauterization of the cervix which had been done elsewhere. Two patients had tuberculosis of the endometrium with resultant pyometra. Two patients had collections of pus in the cervical stumps. One

had had elsewhere a supravaginal hysterectomy. The other patient also had had elsewhere a supravaginal hysterectomy and had had radium therapy to the cervical stump one year before the pyometra was diagnosed.

TABLE VII. PYOMETRA (ADENOCARCINOMA OF THE CERVIX)

		CULTURES			
PREVIOUS THERAPY	NUMBER PATIENTS	NEGATIVE	ANAEROBIC BACTERIA	AEROBIC BACTERIA	MIXED ANAEROBIC AND AEROBIC BACTERIA
None	2	0	1	0	1
X-ray	2	0	2	0	0
X-ray and radium	2	0	0	0	2
Totals	6	0	3	0	3
ADENOACANTHOMA					
None	2	0	2	0	0
SARCOMA OF ENDOMETRIUM					
None	1	0	1	0	0

TABLE VIII. PYOMETRA (ADENOCARCINOMA OF THE ENDOMETRIUM)

		CULTURES			
PREVIOUS THERAPY	NUMBER PATIENTS	NEGATIVE	ANAEROBIC BACTERIA	AEROBIC BACTERIA	MIXED ANAEROBIC AND AEROBIC BACTERIA
None	12	5	6	0	1
Radium	2	1	1	0	0
X-ray	2	1	0	0	1
X-ray and radium	1	0	1	0	0
Totals	17	7	8	0	2

TABLE IX. PYOMETRA (ASSOCIATED WITH OTHER CONDITIONS)

		CULTURES			
PREVIOUS THERAPY	NUMBER PATIENTS	NEGATIVE	ANAEROBIC BACTERIA	AEROBIC BACTERIA	MIXED ANAEROBIC AND AEROBIC BACTERIA
None, stenosis of cervix	30	3	9	6	12
Cauterization of cervix, stenosis	4	0	4	0	0
Totals	34	3	13	6	12
TUBERCULOSIS OF ENDOMETRIUM					
None	2	0	0	0	2
COLLECTION OF PUS IN CERVICAL STUMP					
Supravaginal hysterectomy	2	0	1	1 Brucella suis	0

Bacteriology

Material.—

Table X gives a summary of the cultural findings in 133 patients who had pyometra.

TABLE X. POSITIVE CULTURES AND OXYGEN REQUIREMENTS OF ORGANISMS ISOLATED FROM 133 PATIENTS WITH PYOMETRA

Negative cultures	21
Anaerobic organisms alone	49
Aerobic organisms alone	12
Mixed aerobic and anaerobic organisms	51
Total	133

From the great majority of these patients sufficient pus was obtained for the preparation of direct smears for comparison with the cultural findings. Good correlation was found when the cultural findings were compared with the various morphologic types of bacteria seen on the direct smears.

In our previous report[1] 3 patients were reported from whom cultures were not obtained and 6 patients were reported upon whom only aerobic cultures were done. These 9 patients are not included in the present report.

Collection of Material.—

The method of collection of the pus was described previously.[1] In spite of all precautions taken, the possibility of contamination cannot be excluded. We do, however, feel that the precautions taken made the incidence of contamination minimal. In most patients either the cultures were collected by the bacteriologist, or he was present at the time of the collection. Many of the cultures were collected after the preparation of the patient.

Negative Cultures.—

Twenty-one negative cultures were obtained in a total of 133 patients cultured. Negative cultures occurred in several different types of pyometra. Although sterile pus is not infrequently found in old pelvic infections, several factors could account for some of the negative cultures. First, it is known that a fairly heavy inoculum is necessary to initiate growth of some of the anaerobic bacteria and the number of viable organisms may have been few. Second, some anaerobic bacteria are difficult to cultivate with our present methods of culture. Third, the time elapsing between the collection of the pus and the planting of the cultures may have been too long since exposure to oxygen exerts a lethal effect on some of the anaerobic organisms.

Nonsporulating Anaerobic Bacteria.—

The high incidence of the nonsporulating anaerobic bacteria in pelvic infections of all types and the lack of adequate methods for classifications make detailed classifications of all of these bacteria isolated from pyometra impossible. In preadolescents and in postmenopausal women, these bacteria are normal inhabitants of the vagina. They occur in the vagina in a certain percentage of women during the childbearing age. Work has shown also that this group represents a majority of the bacterial flora of the lower intestinal tract, and is frequently, if not always, present in the upper respiratory tract.

In pyometra and in allied pelvic inflammatory disease, the vagina is the common source of the infection. These bacteria are spoken of as opportunists, and under suitable pathologic conditions become invasive and produce inflammatory disease. It is unfortunate that the vagina seems to be their normal habitat, and in some patients they cannot be eliminated permanently by any methods now known.

Although many of the anaerobic non-spore-forming bacteria were first described more than fifty years ago in infections in obstetric and gynecologic patients, our knowledge at the present, regarding detailed methods of species classification, is hardly more than it was at that time. Most of the work within this group has been done by clinicians, or by bacteriologists, working with single or small numbers of strains. Emphasis has been on naming new species rather than on the study of the group as a whole. As a consequence a number of generic names can be found for a single species, and the number of names and amount of confusion in the literature are enormous. The whole problem needs systematic reinvestigation, particularly in the fields of obstetrics and gynecology.

In the existing chaos some order has been attempted in the sixth edition of *Bergey's Manual of Determinative Bacteriology.*[4] This has been done by excluding all genera and species regarded as inadequately described. Although this is necessary and should be adhered to as a starting point for more complete

investigations, many of the organisms included were studied by investigators using methods that were neither comparable nor complete. However, for the sake of uniformity, the terminology used here is taken from the sixth edition of *Bergey's Manual,* in which the species or generic possibilities are listed.

Practical Terminology.—

In actual practice the bacteriologic laboratory used the terms, *mixed anaerobes, anaerobic streptococci,* and *anaerobic cocci.* The term mixed anaerobes means a mixture of anaerobic cocci and anaerobic nonsporulating bacilli, either gram positive, gram negative, or both. In cultures containing *mixed anaerobes* no effort was made to separate the various morphologic types of cocci and bacilli.

TABLE XI. BACTERIA AND GROUPS OF BACTERIA ISOLATED FROM 112 PATIENTS WITH PYOMETRA AND POSITIVE CULTURES

	POSSIBLE GENERA	NUMBER OF POSITIVE CULTURES
Anaerobic non-spore-forming group (mixed anaerobes)	*Micrococcus* *Diplococcus* *Streptococcus* *Bacteroides* *Neisseria* *Veilonella* *Corynebacterium*	41
	POSSIBLE SPECIES	
Anaerobic streptococci (anaerobic cocci in chains)	*anaerobius* *foetidus* *putridus* *lanceolatus* *micros* *parvulus* *evolutus* *intermedius*	17

TABLE XII. BACTERIA AND GROUPS OF BACTERIA ISOLATED FROM 112 PATIENTS WITH PYOMETRA AND POSITIVE CULTURES

	POSSIBLE GENERA	NUMBER OF POSITIVE CULTURES
Anaerobic cocci (mixed anaerobic cocci)	*Micrococcus* *Diplococcus* *Streptococcus* *Neisseria* *Veilonella*	43
	POSSIBLE SPECIES	
Genus *Corynebacterium* (diptheroids)	*pseudodiptheriticum* *xerose* unidentified	50

In Table XI are shown the generic possibilities when this term, mixed anaerobes, is used as defined. The term anaerobic streptococci was used when only anaerobic cocci were found which formed chains and morphologically could be

classed as streptococci. The species possibilities are shown in Table XI. The term anaerobic cocci was used when the anaerobic broth cultures showed only a mixture of anaerobic cocci, either gram positive, gram negative, or both, of varying morphologic types. The generic possibilities are shown in Table XII.

Incidence of Anaerobic Bacteria.—

In Table X is shown the incidence of anaerobic bacteria in the group of 112 patients whose cultures showed growth. One hundred of the 112 positive cultures showed anaerobic bacteria and in 49 cultures there were no associated aerobes. This emphasizes the importance of the endogenous, ascending type of infection in the common forms of pyometra.

Anaerobic Non-spore-forming Group.—

Mixed anaerobes occurred in 41 cultures. The most common bacilli encountered in these mixed cultures belonged to the genus Bacteroides. Bacilli belonging to this genus occur in the literature under several generic terms and the genus itself is ill defined. Some strains were extremely pleomorphic, and because of extreme pleomorphism, could have been classed as *Bacteroides funduliformis*. These bacilli constitute a distinct part of the bacterial flora of the colon and are frequently found in pelvic infections of all types.

Species identification is confused. In our own laboratory these bacilli have exhibited a variety of morphologic and cultural variations. Although pure cultures of Bacteroides have been isolated in our own laboratory in other types of pelvic infections, in pyometra, they always occurred in symbiosis with anaerobic cocci of various types. Most strains of Bacteroides, particularly the pleomorphic varieties, produce gas and a foul odor in anaerobic meat media. In addition to Bacteroides, anaerobic Corynebacteria, or diphtheroid bacilli, were not infrequently seen in mixed cultures. Anaerobic strains of Corynebacteria are known to exist and have been described, but descriptions are so inadequate that they are not listed in *Bergey's Manual.*[4]

Methods of Culture.—

Most infections due to the nonsporulating anaerobic bacteria are mixed infections. Experience has shown that these bacteria grow best in symbiosis. If blood plates alone are used for primary cultures a certain amount of selection occurs and some of the morphologic types seen in direct smears will not be cultured. On the other hand some anaerobic broth media, particularly thioglycollate, may show selectivity which allows aerobic organisms along with the more hardy anaerobic strains to overgrow some of the anaerobes which are more fastidious in their growth requirements. For this reason we have found that an anaerobic meat medium is best for primary culture as less selectivity and more correlation with direct smear finding are obtained.

The formula for this medium is a slight modification of one originally described by Lepper and Martin[5] which utilizes neutralized beef heart and has a final pH of approximately 7.4. Cultures in this medium have the advantage that a petrolatum seal is used. This sealing permits the detection of gas formation. Gas formation is of importance in the differentiation of some of the anaerobic bacteria from morphologically similar aerobes. For testing for anaerobiosis, and isolation for study, blood plates and the hydrogen replacement method were used.

No description of the aerobic culture method is necessary since most of the aerobic plate formulas in common use will prove satisfactory for aerobic cultures.

Anaerobic Streptococci.—

Of all the anaerobic bacteria, the streptococci are the most frequently isolated and probably the most important. They were thought to be the only

anaerobes present in 13 cultures, but were present in most of the cultures positive for anaerobic cocci and mixed anaerobes. Many of the anaerobic streptococci produce gas and a foul odor in culture. This odor is quite similar to the odor found in patients with advanced infected carcinoma of the cervix.

Anaerobic Cocci.—

Anaerobic cocci, not associated with anaerobic bacilli, occurred in 43 cultures. The generic possibilities are shown in Table XII. In general these cocci are morphologically identical with aerobic species of the same genus, but the diplococci rarely show capsule formation and the veilonella are minute gramnegative cocci with no aerobic species listed.

Bacteria Other Than the Nonsporulating Anaerobes.—

The three varieties of aerobic streptococci occurred infrequently as compared with the anaerobes; *Streptococcus pyogenes* in 9 cultures; *Streptococcus viridans* in 7; and nonhemolytic streptococci in 9 (Table XIII).

TABLE XIII. BACTERIA AND GROUPS OF BACTERIA ISOLATED FROM 112 PATIENTS WITH PYOMETRA AND POSITIVE CULTURES

	NUMBER OF POSITIVE CULTURES
Streptococcus—nonhemolytic group	9
Streptococcus—viridans group	7
Streptococcus—pyogenes group	9
Micrococcus pyogenes var. albus	7
Micrococcus pyogenes var. aureus	5
Escherichia coli	5
Proteus vulgaris	1
Pseudomonas aeruginosa	1
Brucella suis	1
Mycobacterium tuberculosis	2
Clostridium welchii	2
Fusospirochetal group	1

Micrococcus pyogenes var. *albus* was isolated 6 times and the *aureus* variety 5 times.

The most common aerobes isolated were the Corynebacteria or diphtheroids. These organisms commonly occur in the vagina in the absence of infection, and seem to be a part of the vaginal flora. They are seldom seen in cultures from pyometra in large numbers and the pathogenicity of this group is highly questionable.

Escherichia coli were isolated from but 5 patients. One culture showed *Proteus vulgaris* and one *Pseudomonas aeruginosa.*

Cultures on two patients showed spore-forming anaerobic bacilli, which were identified as *Clostridium welchii.*

Two patients with tuberculous endometritis and associated pyometra had positive cultures for *Mycobacterium tuberculosis.*

One patient showed fusospirochetes in direct smear and on culture had associated mixed anaerobes.

One patient with a collection of pus in the cervical stump had a positive culture for *Brucella suis.*

Summary

1. A series of 133 patients with pyometra is reported.

2. The clinical groupings and data are presented in tables.

3. The incidence of pyometra is higher than the report indicates, since only those patients were reported on whom cultural studies were done. The incidence

will increase with the realization that it can be diagnosed only by proving patency of the endocervical canal of the uterus *or of the cervical stump*.

4. Pyometra in this series occurred most commonly in patients who had received irradiation therapy for malignant neoplasms of some part of the uterus. It is also significant that all patients who developed pyometra with *untreated* malignant neoplasms of the uterus were in the postmenopausal age group.

5. The cultural findings in the various clinical groupings are given in table form. The classification of the nonsporulating anaerobic bacteria is discussed.

6. The importance of the anaerobic organisms in pyometra is clearly shown. In the 133 patients, 21 negative cultures were reported. In 49 patients anaerobic organisms alone were cultured; in 51 patients mixed aerobic and anaerobic organisms were cultured. In short, in 112 positive cultures for the entire series, 100 cultures showed anaerobic organisms and but 12 cultures showed aerobic organisms alone.

7. Twenty-one negative cultures were reported. In 69 patients with squamous-cell carcinoma of the cervix there were 11 (15.8 per cent) negative cultures. In 6 patients with adenocarcinoma of the cervix there were no negative cultures. In 17 patients with adenocarcinoma of the endometrium there were 7 (41.7 per cent) negative cultures. In 30 patients with "spontaneous" pyometra due to endocervical stenosis, there were but 3 (10 per cent) negative cultures; 29 of these 30 patients were postmenopausal.

8. No patient in this series had pyometra which was due to hormonal therapy.

9. No deaths occurred in this series as a result of pyometra.

10. Much investigative work must be done before the anaerobic organisms can be classified properly. The response of aerobic organisms to the various chemotherapeutic and antibiotic agents has been well studied. However, the effect of these agents on the bacteria of the nonsporulating anaerobic group is still unsatisfactory and of controversial nature.

11. Judgment as to the time after the evacuation of pyometra to use the curette, radium, or x-ray, or to operate, is difficult. Adequately controlled bacteriologic studies should aid in answering some of the problems which pyometra presents to the clinician.

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Discussion

DR. FRANKLIN L. PAYNE, Philadelphia, Pa.—The problem of pyometra presents three major facets: the circumstances under which it occurs, the bacteriology, and the choice of management. Dr. Carter, in his scholarly presentation, has reported 133 patients with pyometra and to that number we can add 118 patients who have been treated at the Hospital of the University of Pennsylvania during the past twenty years. As to the first facet, the predisposing conditions, both series offer sufficient material for analysis. As to the second,

the bacteriologic aspects, Dr. Carter is abundantly equipped while we are woefully lacking. As to the third, the clinical management, Dr. Carter restricts his remarks to the following statement, ''Judgment as to the time after the evacuation of pyometra to use the curette, radium, or x-ray, or to operate, is difficult. Adequately controlled bacteriologic studies should aid in answering some of the problems which pyometra presents to the clinician.'' Based upon our clinical experience with 118 patients we will try to make more specific deductions.

First, to consider the conditions under which pyometra occurs. The essayist states that his patients do not represent the true incidence of pyometra in his clinic. Many other patients with pyometra were not included because of the failure to obtain properly the pus for culture. It is unfortunate that the latter cases are not included for such inclusion would strengthen the clinical portion of his study. Dr. Carter's reported group is divided as follows: those associated with cervical malignancy 75 (57 per cent), with endometrial malignancy 20 (15 per cent), and not associated with malignancy 38 (28 per cent). Our cases are divided similarly: those associated with cervical malignancy 47 (40 per cent), with endometrial malignancy 37 (31 per cent), and not associated with malignancy 34 (29 per cent). In brief, 71 per cent of Dr. Carter's patients and 72 per cent of our patients with pyometra had uterine malignancy. Since this is the most frequent accompaniment of pyometra, the clinician must prove or disprove its presence in every case prior to the institution of definitive therapy. The group not associated with malignancy present many predisposing factors. In Dr. Carter's 38 nonmalignant patients, 30 collections attended spontaneous cervical stenosis (29 of which were postmenopausal), 4 followed postcauterization stenosis of the cervix, 2 were due to tuberculosis, and 2 to pyocervices. In our group of 34 cases of nonmalignant pyometra (30 of which were postmenopausal) 15 were due to spontaneous cervical stenosis, 10 to previous treatment of the cervix (cauterization, conization, or amputation), 5 to submucous polyps or myomas, and 4 followed intrauterine radiation for benign conditions. Of the nonmalignant pyometra, comprising approximately 30 per cent of both groups, the frequency of causes presented in the following order: spontaneous postmenopausal cervical stenosis, obstruction following cervical treatment, submucous myomas, or polyps, radiation therapy for benign conditions, tuberculous endometritis, and infection in the retained cervix.

As to the bacteriology, Dr. Carter is far ahead of us, for we have not done routine anaerobic cultures while all of his cases were cultured both aerobically and anaerobically. The anaerobic organisms were found in 100 of these, half of which demonstrated aerobic organisms also and only 12 showed aerobes alone. Based on Dr. Carter's bacteriologic findings, we must conclude that both aerobic and anaerobic cultures are necessary for complete bacteriologic evaluation. While these figures suggest the usefulness of such studies in the clinical management of patients with pyometra, the necessity for the routine employment of such exhaustive investigation remains dubious. The practical importance of his investigation would have been strengthened by the inclusion of those patients who did not receive these studies, with enumeration of the difficulties that followed the lack of bacteriologically controlled management. We must heed, however, Dr. Carter's statement that no deaths occurred in his series as a result of pyometra. While no deaths occurred in our series as the direct result of pyometra, we were not so fortunate in the management of this condition.

In 138 instances of pyometra, in 118 patients, in the admitted absence of exhaustive bacteriologic control, pyometra occurred with cervical malignancy in 51, with endometrial malignancy in 47, and with nonmalignant conditions in 40 instances. The management of the pyometra consisted of either simple drainage, usually with a tube, curettage with drainage, curettage with local radiation, evacuation with local radiation, or hysterectomy. Of those treated by drainage, numbering 44, serious trouble arose in one, a patient with advanced endometrial cancer. Following curettage and drainage, serious trouble arose in 3 of 59 patients. With curettage and local radiation we got into serious difficulty with 3 of 24 patients. With local radiation alone (all of these patients had been treated by x-ray therapy previously) there were no complications. Following hysterectomy, one patient died from pneumonia. Six of the 8 serious sequelae followed curettage and 2 of the 3 deaths followed this procedure. From this study the following deductions seem to be justified: the safest

management of pyometra consists of evacuation and tube drainage, to await a more favorable time for diagnosis and/or treatment, as indicated by the clinical picture of the patient. The presence of pyometra contraindicates either immediate curettage or the local application of radium, with one exception. If pyometra is discovered shortly after x-ray therapy, the prompt local application of radium seems to be safe possibly because of the sterilizing influence of the recent radiation.

It seems to us that the adoption of a policy in line with these deductions will permit the safe management of pyometra and its associated conditions without the need for such exhaustive bacteriologic studies as those suggested by Dr. Carter.

DR. HOUSTON EVERETT, Baltimore, Md.—Dr. Payne, in his discussion of this paper, pointed out the danger of curettage but I would like to ask, when the diagnosis of pyometra has been established, what is the procedure for curettage and when should it be done in relation to the diagnosis of pyometra?

DR. CARTER (Closing).—I thank Dr. Payne for his discussion. The question of the clinical value of this bacteriology to us is no longer a question. Anaerobic and aerobic cultures will add much to our information concerning the pathologic conditions we will continue to find in the pelvis. We know little about the anaerobic organisms despite the work done in the past 20 years. We do know that these same organisms are found in pelvic abscesses and that we have true difficulty in treating these abscesses. An attempt to classify the anaerobic organisms should be continued. In the anaerobic non-spore-forming group (mixed anaerobes), under the possible genus, Bacteroides, we have an organism which has in the recent literature shown its ability to cause serious trouble.

We also think that careful maintenance of endocervical patency will prevent the inadvertent removal by vaginal or abdominal hysterectomy of a uterus with pyometra. This prevents an added hazard to the patient and also saves the operator embarrassment. In answer to Dr. Everett's question: When we evacuate pyometra we like to wait 3 to 4 weeks before doing any operative or radium procedure upon that patient. We also like to check that patient with our bacteriologist who is an integral part of the team which decides what should be done for her. The bacteriologist should be at the table with the patient when pyometra is evacuated. The procedure of sending a culture tube to the laboratory is a wrong procedure, and cultures made from material transported in this manner are often not complete and lead to inaccuracies.

We also feel strongly that adequate bacteriologic diagnosis and controls will cut down on the indiscriminate use of the antibiotics in pelvic infections.

CLINICAL CONSIDERATIONS OF BENIGN OVARIAN CYSTOMAS*

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PRESERVATION of ovarian tissue is essential and desirable. This would seem to indicate ovarian resection rather than oophorectomy when neoplasms are benign, and suggests scrutiny of indications for the so-called prophylactic removal of ovaries.

In an effort to determine how often preservation of ovarian tissue proves to have been an unwise course, we have been following a number of women operated upon for ovarian neoplasms in the Buffalo General Hospital during the years 1936 to 1947, inclusive. The pathologic conditions encountered in this series can be briefly summarized as follows:

Excluding dysfunctional or hemorrhagic, follicular or luteal "cystic ovaries," ovarian tumors were removed from a total of 1,112 women during the 12-year period surveyed (Table I).

TABLE I. OVARIAN TUMORS (EXCLUDING INFLAMMATION), BUFFALO GENERAL HOSPITAL, 1936-1947

Malignant			16.2%	180 cases
Potentially malignant			4.4%	49 cases
Endometriosis with "chocolate cyst"			26.4%	294 cases
Benign cystomas			47.3%	
Simple	20.3%	226		
Cystadenomas	14.9%	166		
Dermoids	12.0%	134		526 cases
Fibroadenomyomas			0.7%	8 cases
Brenner			0.5%	5 cases
Fibromas			4.5%	50 cases
Totals			100.0%	1,112 cases

Texts and current literature usually state that 10 to 15 per cent of ovarian neoplasms are malignant. In this series, 180 patients (16.2 per cent) were considered to have unquestionably malignant tumors.

In a second group, 49 tumors are classified as potentially malignant. Only two of 22 teratomas were histologically malignant and the remaining 20 have proved clinically benign. Of 14 patients with granulosa-cell tumors, 3 died with abdominal carcinomatosis, 3 are living with recurrences of granulosa-cell carcinoma; and 4 have remained clinically free of recurrence for a number of years. Of 5 cases of dysgerminoma followed, 2 have exhibited a malignant character to date.

In our material the ovarian tumor most frequently operated upon is the chocolate cyst associated with endometriosis. Benign cystomas, including

unilocular simple cystomas, multilocular cystadenomas, and dermoids, totaled 47.3 per cent in the 1,112 cases. There were 50 fibromas, 8 classified fibroadenomyomas and 5 Brenner tumors, in the series.

A frequently quoted generalization suggests that an ovarian tumor discovered in a woman over 50 years of age should be regarded as malignant. We noted that 68.2 per cent of the malignant tumors and 31.2 per cent of the cystomas considered benign were removed from women "over 50." Preoperative irradiation has been suggested when an ovarian neoplasm is discovered in a woman "over 50." We were interested to learn that in 218 such instances only 131, or 60 per cent, of the tumors proved malignant. If there is a 40 per cent chance that a pelvic tumor is not malignant and a possibility that the suspected ascites may not be secondary to ovarian carcinomatosis, we do not consider preoperative irradiation advisable.

Dermoid Cystomas

A few textbooks gave the impression that dermoid cystomas may frequently be found in both ovaries. Recent editions have stated that "less than 25 per cent" occur bilaterally, or that dermoids are "usually unilateral." We found dermoids to involve both ovaries simultaneously in 16, or 11.9 per cent, of 134 patients. In an effort to determine the ultimate incidence of bilateral involvement, we have followed 90 women after removal of one ovary for a dermoid. Six years after the unilateral oophorectomy, one developed a similar tumor in the remaining ovary. To date 55 others have been followed more than six years, but no other dermoids have developed, suggesting that the risk of bilateral involvement must approximate 12 per cent.

A review of 1,149 ovarian tumors surgically treated at the Helsinki University Clinic of Gynecology[1] states that dermoids were bilateral in 10.4 per cent of 208 cases. From these data it would appear that the chance of a carefully preserved other ovary developing a dermoid eventually to indicate a second laparotomy seems too small to justify its "prophylactic" removal. However, the fact that both ovaries are involved in 10 to 12 per cent of cases does seem to indicate careful palpation and bisection of the opposite ovary even when the latter appears normal.

In this connection it is admitted that the spilled contents of a dermoid may prove irritating to the pelvic peritoneum but we believe that is particularly true only when the dermoid has become necrotic as a result of torsion of the pedicle. If a little care is taken to protect the adjacent peritoneum, oophorectomy is not often necessary in the treatment of dermoid cystomas. The larger cysts can be resected and unsuspected smaller ones should be identified and excised after bisection of the opposite ovary.

Simple Cystomas

Cystomas considered benign, "simple" cystomas, cystadenomas, and dermoids totaled 526, or 47.3 per cent, of the tumors reviewed. Nearly one-half of this group were unilocular, serous, or pseudomucinous but "simple" cystomas with a grossly smooth lining. Some were quite large. Twenty-three per cent were discovered in patients over 50 years of age; 6.6 per cent were bilateral when discovered; and in one instance the other ovary was largely replaced by a fibroma.

After a simple cystoma had resulted in the removal of one ovary, 69 women have been followed, 52 for periods longer than five years. In two instances enlargement of the preserved ovary indicated a second laparotomy within three years. At the second operation one had a similar simple cystoma,

one a chocolate cyst in the remaining ovary. In both instances the developing pathology in the preserved ovary might have been evident if that normal-looking other ovary had been bisected at the time of the initial laparotomy. We rarely observe circumstances suggesting the length of time required for the development of a benign cystoma. However, in one case both ovaries were considered normal when hysterectomy was performed on Oct. 25, 1938, yet a grapefruit-sized simple cystoma replaced one ovary at a second laparotomy on July 13, 1939. It seems probable that simple cystomas develop more rapidly than the multilocular and dermoid varieties, but unfortunately few reliable data are available on this point.

It was also interesting to learn that among the 69 women followed there were 32 under 35 years of age when one ovary was removed. To date, although they have been followed an average of eight and three-fourths years, only 5 of the 32 have borne children after unilateral oopherectomy for a simple cystoma.

Cystadenomas, pseudomucinous and serous combined, numbered 166, or 14.9 per cent, of the ovarian tumors. This includes both the papillary and nonpapillary varieties of multilocular cystadenoma which total 31.6 per cent of the benign cystomas in the series.

Pseudomucinous Cystadenomas

The majority, 53 of 84 cases, or 63.1 per cent of pseudomucinous tumors, occurred in women under 50 years of age. In 14 of the 84 cases, or 16.6 per cent, both ovaries were removed. In only 5 of the 84, the cystoma was bilateral. In one case a dermoid and in another a simple cystoma in the opposite ovary resulted in bilateral oophorectomy in both instances. In only 7, 8.3 per cent, of the 84 cases, prophylactic removal of the other ovary was considered advisable. Two of this group were 46 and 49, the remaining 5 were over 50 years of age.

Sixty-four patients with pseudomucinous cystadenomas of one ovary have been followed after unilateral oophorectomy. The cause of one death is unknown, 6 died of cardiovascular disease or malignancies unrelated to an ovarian tumor. Among 38 followed more than five years, one after four years was re-operated upon for a pseudomucinous cystoma in the remaining ovary. Among the 64 with one ovary preserved there were 23 women under 35 years of age. Seven of this group, after unilateral oophorectomy, have to date carried a total of 15 babies to term.

We are inclined to be more apprehensive of the patient's future when gross sectioning of the tumor reveals areas of papillary lining. Sixteen women have been followed after removal of pseudomucinous cystadenomas having grossly papillary linings. One died of a primary carcinoma of the pleura after two years, one died of unknown cause eight years after oophorectomy. The remaining 14 have been followed three to twelve years and none to date has developed a suggestion of recurrence, metastasis, or pseudomyxoma peritonei. Many textbooks state that perhaps 5 per cent of pseudomucinous cystadenomas become malignant but that tendency is not evident among the tumors in this series considered benign at the time of operation.

In addition to the 84 cases of pseudomucinous cystadenoma reported, 5 women were observed who presented the widespread implantation and mucinous free fluid characteristic of pseudomyxoma peritonei. In all 5 instances extensive peritoneal implantation was evident the first time the abdomen was opened. Three, aged 60, 55, and 54 years, respectively, developed large quantities of free mucinous fluid, extensive adhesions, recurring

intestinal obstruction, and died within 22 months of the time the abdomen was first opened. One woman, first operated upon in 1930 at 28 years of age, and one first operated upon in 1933 at 21 years of age, are still living with innumerable varying-sized calcified nodules, and adhesions matting bowel into masses throughout the abdomen. It was reassuring to learn that except when free fluid and extensive implantation were evident at the time of the initial oophorectomy, no case of pseudomyxoma peritonei followed removal of a pseudomucinous cystadenoma.

Serous Cystadenomas

In this series 38 of 82 cases, or 46.3 per cent, of cystadenoma with a serous content occurred in women "over 50." However, the patients' age was not the factor accounting for bilateral oophorectomy in this group. In only 18 of the 38, or 47.4 per cent of the cases "over 50," both ovaries were removed. Gross sectioning of the cystadenoma at the time of surgery and discovery of a papillary lining more frequently prompted removal of both ovaries. In 60 cases with papillary linings, 24, or 40 per cent, had bilateral oophorectomy. On the other hand, of the 22 cases in which the multilocular serous cystoma had a smooth lining, in only 6, or 27.3 per cent, were both ovaries removed.

The follow-up indicates little difficulty when a serous cystadenoma involves only one ovary. We might consider this benign course due in part to the fact that in 17 of the 82 cases, while only one ovary was involved, both ovaries were removed. Even though in 13 of the 17 cases the tumor exhibited a grossly papillary lining, all 13 patients are living and 11 have been followed for periods of 4 to 11 years.

Cystadenomas with a serous content are generally regarded as the least predictable of the benign cystomas. However, even with this type of tumor we could find little evidence that prophylactic removal of an opposite normal-looking ovary is justified. When only one ovary was involved and the opposite ovary was preserved in 50 cases, even though the cystadenoma exhibited a grossly papillary lining in 38, 76 per cent of the group, the follow-up indicates a clinically benign course. To date, 3 of these women have died at ages 70, 63, and 50 years, 9 have been followed for more than 10 years, with no evidence of tumor in the preserved other ovary.

When only one ovary was involved, 8 of the 50 patients with the opposite ovary preserved were under 35 years of age. To date, 4 of the 8 have become pregnant and have carried a total of 5 babies to term.

The apprehension frequently voiced regarding the potentialities of apparently benign serous cystadenomas is undoubtedly due to experiences similar to those evident in Tables II and VI. When both ovaries are involved and the tumor shows a grossly papillary lining, either the surgeon's impression at operation or a pathologist's diagnosis based on routine sectioning may eventually prove to have been misleading.

TABLE II. SUMMARY, 64 SEROUS PAPILLARY CYSTADENOMAS FOLLOWED

13	One ovary involved	Bilateral oophorectomy	0 Proved malignant
38	One ovary involved	Unilateral oophorectomy	0 Proved malignant
13	Both oovaries involved	Bilateral oophorectomy	3 Proved malignant

We have been able to follow 13 of the 15 cases of bilateral cystadenomas with grossly papillary linings. Two patients died of cardiovascular disease three and five years after operation. Three died, five, seven, and nine years after operation with recurring pelvic tumor diagnosed on reappearance as

adenocarcinoma, "most probably of ovarian origin." In all three of the latter cases, the original tumors were considered "not malignant" and both ovaries had been removed. Five other women with apparently similar bilateral ovarian involvement are free of disease 4 to 11 years after oophorectomy. In 2 of the 5 long survivals, peritoneal implantation had been evident at the time of operation and the operator had considered wide resection indicated for a suspected malignancy, yet the bilateral tumors had been reported benign and the clinical course has agreed with the histology reported.

To summarize, 64 patients with serous, papillary cystadenomas have been followed after operation (Table II). In 13 cases, one ovary was involved, but bilateral oophorectomy was performed and there has been no recurrence of the pelvic tumor. In 38 cases, one ovary was involved, the opposite ovary was preserved, and there have been no recurrences. However, of 13 women with bilateral papillary cystadenomas, even though both ovaries were removed, in 3 instances recurrent pelvic tumor appeared both histologically and clinically malignant.

It has been interesting to compare our data with those recently published from the Helsinki University Clinic (Table III). They noted 10.4 per cent of dermoids occurring bilaterally, our figure is 11.9 per cent. Simple cystomas were bilateral in 9.3 per cent of their series, and in 6.6 per cent of our cases. Pseudomucinous cystomas occurred in both ovaries in 9.3 per cent of the cases at Helsinki and in 7.2 per cent of our series. Serous cystadenomas occurred bilaterally in 12 per cent of their patients, and in 18.3 per cent of the women in our series.

TABLE III.   BENIGN OVARIAN CYSTOMAS, INCIDENCE OF BILATERAL OCCURRENCE

	DERMOIDS	SIMPLE CYSTOMAS	PSEUDOMUCINOUS CYSTADENOMAS	SEROUS CYSTADENOMAS
Helsinki series	10.4%	9.3%	9.3%	12 %
Buffalo General	11.9%	6.6%	7.2%	18.3%

Comment

Our material suggests little basis for the tendency to regard all cyst-adenomas as "potentially" malignant, for there is little to justify a "guarded prognosis" in the follow-up of the great majority of cases. Particularly when the lining of a cystoma appears grossly papillary, gynecologists have been prone to perpetuate an unjustified fear that the tumor may ultimately prove to be malignant, even though sections show it to be benign. Our observations suggest that for every histologically benign tumor which proves clinically malignant we will see grossly malignant-looking, implanting neoplasms that ultimately prove to be as benign as the histologic sections indicated. Follow-up study has convinced us that routine histologic sections of even the large cystomas provide a more reliable indication of the prognosis than can be prophesied from the gross appearance of the tumor.

Several considerations account for the frequency of so-called prophylactic oophorectomy during the performance of indicated pelvic surgery. A carefully preserved ovary may develop pathology requiring a second laparotomy. Continued ovarian function has been suspected of providing a background favoring the eventual development of endometrial carcinoma. We frequently hear that routine removal of the ovaries whenever pelvic laparotomy is indicated for women "over 40" or "over 50" constitutes the most effective method of decreasing deaths due to ovarian malignancy. Thus it seems advisable occasionally to review the consequences of preserving ovarian tissue.

Statistics from the Bureau of Cancer Control,[2] Department of Health of the State of New York, indicate that each year 11.3 women among each 100,000 females develop ovarian cancer, if the ovaries are not removed. I know of no figures suggesting that the incidence of ovarian cancer is higher in women developing fibroids or benign adnexal lesions indicating pelvic laparotomy "over 40." Evidently we are not dealing with a predisposed group when operating on women with benign pelvic disease. Therefore, even if we assume that the average woman will have a life expectancy of 30 years after the laparotomy when prophylactic oophorectomy is to be considered, the possibilities that she will eventually develop ovarian cancer do not exceed four per 1,000. Such an incidence of ovarian malignancy does not seem to warrant removal of normal ovaries purely as a cancer-preventing measure. This is particularly true if need of a hysterectomy indicates the laparotomy and both ovaries are normal.

When one ovary is involved in a neoplastic process the ultimate chance of the same or a different type of tumor developing in the other ovary has suggested its removal on a prophylactic basis. While such decisions will always be influenced by the patient's age, they also depend upon our knowledge of the relative frequency with which the varying types of ovarian neoplasms involve both ovaries. The best management would seem to require prompt recognition of the type of cystoma and of the potentialities of the neoplasm discovered. Moreover, we might reason differently than merely to doubt that the incidence of bilateral involvement warrants prophylactic removal of the other ovary when it is apparently normal. Ovarian tumors do ultimately involve both ovaries—frequently enough to contraindicate oophorectomy when only one side is involved—if resection of the cystoma can possibly be accomplished. Obviously the advantages of resection rather than oophorectomy will be realized only in those instances in which the apparently normal "other" ovary eventually requires removal.

Among surgeons, gynecologists comprise a group fully aware of the advantages of preserving the ovary. Oophorectomy can be quickly accomplished and, by comparison, ovarian resection is fussy surgery. We all understand the temptation to do the quicker, neater job, especially when the woman has another normal-looking ovary. As a result the advantages of ovarian resection often receive little consideration, unless the patient has previously lost an ovary. When one ovary has been removed, the operator always makes an effort to save a part of the opposite ovary. Is it not evident that we should approach an initial oophorectomy, as well as a single remaining ovary, with a consistent desire to conserve ovarian tissue?

Laparotomy is indicated for ovarian tumor in approximately 10 per cent of the surgery performed by gynecologists. When only one side is involved, we should not assume that the normal-looking "other" ovary is actually free of early tumor unless we carefully palpate and bisect it—before we decide what to do to the grossly involved ovary. Ineffective efforts at repair, or performance of hysterectomy when the indications are debatable, seem minor offences compared to the effects of an eventual castration when it could have been avoided. I believe we should emphasize the desirability of resection in the treatment of benign cystomas as consistently as we condemn the removal of ovaries for dysfunctional cystic change.

Summary

How often does the preserved "other ovary" develop a tumor requiring a second laparotomy? Our observations can be summarized as follows (Table IV):

TABLE IV. PATHOLOGY IN THE REMAINING OVARY

UNILATERAL OOPHORECTOMY FOR	NUMBER OF PATIENTS FOLLOWED		REMAINING OVARY REMOVED	PATHOLOGY OF SECOND OVARY
Dermoid	90	55 for 6+ yr.	1 in 6 yr.	Same
Simple cystoma	69	52 for 5+ yr.	1 in 2 yr.	Same
			1 in 3 yr.	"Chocolate cyst"
Pseudomucinous cystadenoma	64	38 for 5+ yr.	1 in 4 yr.	Same
Serous cystadenoma	50	31 for 5+ yr.	——	——

Ninety women with dermoids treated by unilateral oophorectomy have been followed, 55 for more than six years after operation. One patient, during the sixth postoperative year, developed a dermoid in the remaining ovary.

Sixty-nine women with one ovary removed because of a simple cystoma have been followed, 52 for more than 5 years. One patient, two years after oophorectomy, developed a similar cystoma in the other ovary and one other, after three years, developed a typical chocolate cyst in the preserved "other" ovary.

Sixty-four women with one ovary removed because of a cystadenoma with pseudomucinous content have been followed, 38 for more than five years. One patient, after four years, developed a similar tumor in the opposite ovary.

Fifty women with one ovary preserved after removal of a serous cystadenoma on the opposite side have been followed, 31 for more than five years. None has to date developed a tumor in the preserved ovary, nor evidence of recurrence of tumor in the pelvis.

One hundred seventy-six patients have been followed more than five years after unilateral oophorectomy for supposedly benign cystomas (Table V).

TABLE V. SUMMARY

In 176 patients followed 5+ years to date, 2.3 per cent incidence of pathology in the remaining ovary.

Four have required reoperation for tumors in the preserved "other" ovaries, two, three, four, and six years after their initial laparotomies.

We have observed to date only a 2.3 per cent incidence of pathology in the remaining "other" ovary.

Finally, to summarize observation of 80 cystadenomas exhibiting grossly papillary linings, 16 with a pseudomucinous and 64 with serous content have been followed (Table VI). Three of the serous cystomas, all 3 multilocular papillary and occurring bilaterally, have recurred as malignant tumors. To date, 77 others have experienced a clinically benign course.

TABLE VI. SUMMARY

80 cystadenomas with grossly papillary lining followed
(16 pseudomucinous)
(64 serous)
3 serous, occurring bilaterally, recurred as malignant tumors.
77 others—clinically benign course.

Conclusions

When ovarian tumors are discovered in women over 50 years of age 40 per cent prove to be benign.

The incidence of the bilateral occurrence of benign ovarian cystomas or the ultimate incidence of ovarian malignancy does not warrant the removal of an opposite normal-appearing ovary merely as a prophylactic measure.

The chance of bilateral pathology, not grossly appreciable but already developing in the other ovary, indicates careful inspection, palpation, and bisection of the opposite ovary before it can be regarded as normal and uninvolved.

The chance of the development of pathology in the opposite ovary at a later date should cause us to favor resection of benign cystomas, rather than oophorectomy, whenever it is possible to preserve even a shell or portion of ovary on the involved side. The possibility of continued oogenesis adds reason to preserve even small portions of any ovary. Moreover, in our material to date, we have found nothing to suggest the recurrence of an ovarian neoplasm in the ovarian tissue remaining after resection of a benign cystoma.

The danger of peritoneal implantation from a papillary cystadenoma opened at surgery, like the danger of disseminating endometriosis by the resection of a chocolate cyst, appears to have been overemphasized.

Resection of the ovary should be considered more often and oophorectomy employed less routinely in the management of benign ovarian cystomas.

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Discussion

DR. WILLIAM MENGERT, Dallas, Texas.—Dr. Randall has presented us with much informative material. Few men have access to a well-controlled and documented series of 1,112 women from whom ovarian tumors were removed. The theme of Dr. Randall's paper is conservation of ovarian tisue. This is a far cry from the days of Battey's operation when castration was believed to cure nearly all the ills of women. Such was the popularity of this procedure that many general surgeons of today regard the ovary most cavalierly. It has even been said facetiously that no ovary is ever good enough to save and no testicle sufficiently diseased to remove. Moreover, we have seen the curious paradox, on the one hand, of needless sacrifice of normal ovaries at routine laparotomy for confused indications and, on the other hand, a singular reluctance to remove them in the relatively rare presence of known pelvic malignancy.

During five years, 1,320 ovaries passed through the Department of Pathology of a Dallas hospital; 993, or 75 per cent, were normal or contained physiologic cysts. In contrast, in the same city during a ten-year period there were 294 women with histologically proved ovarian malignancy, of whom only seven received bilateral salpingo-oophorectomy and total hysterectomy. The remainder received a less extensive operation. I do not believe these conditions are peculiar to Dallas. Quite obviously normal ovaries are removed unnecessarily, the general surgeon confusing physiologic derangements with serious tumors. Hence the sacrifice of huge quantities of normal ovaries on insignificant indication in Dallas and, I presume,

in the nation. The same general surgeon, on the other hand, suddenly becomes squeamish and overly considerate of the opposite ovary when confronted with a malignant ovarian neoplasm. Thus, in a situation which occurs infrequently, he jeopardizes the patient's chances by ultraconservatism. For these reasons Dr. Randall's paper is timely and the facts contained therein deserve wide publicity.

The low incidence given of recurrence or subsequent development of tumor in the remaining ovary, 2.3 per cent, amply justifies its retention. Even if tumor does develop and a second laparotomy is required, it would seem that the second operation is a small price to pay for the use of an ovary for several years.

What of the physiology of the ovary of unilaterally oophorectomized women? Whitelaw performed several hundred endometrial biopsies on about forty such women and found evidence of ovulation in more than 95 per cent of menstrual cycles. Obviously, one ovary adequately performs the work of two.

We all applaud the ideas and the position of the essayist, particularly with regard to premenopausal women. I should like to ask him about the postmenopausal patient. Does he feel there is use for the ovary after the menopause? In other words, is there the same vital need for ovarian conservation in such women?

From the clinical standpoint I should like to re-emphasize a rule constantly repeated to my residents: when a surgeon at laparotomy removes any part of the female genital apparatus for neoplasia, it is his duty before he closes the abdomen to take every reasonable step at his command to insure that the remaining tissue is benign.

DR. LUDWIG EMGE, San Francisco, Calif.—I have listened with much interest to the very pertinent remarks made by Dr. Randall and Dr. Mengert in defense of the preservation of the normal ovary. I have consistently adhered to the belief that there is no good reason to remove what appears to be a normal ovary just because a benign cyst occupies the other ovary or because the uterus requires removal. If the Good Lord in his wisdom had placed the ovaries in as conspicuous a place as he did the testes I am sure that the ovary would fare better in pelvic surgery. Only twice in my long experience have I been compelled to remove an ovary for cancer some years after hysterectomy. A few times I have been forced to remove the remaining ovary because of the growth of a cystadenoma, or for pain, or for residual endometriosis, but I have not considered this a serious commission, or omission, in comparison to the many hundreds of ovaries saved. Even the preservation of ovaries in the presence of endometriosis has been a fruitful experience for my patients as well as for me. I have never seen any major disturbances in the postmenopausal ovary left in place after vaginal hysterectomy, yet it has been argued that removing ovaries eliminates the risk of cancer and therefore is justified. The fallacy and the danger inherent in such a philosophy are evident when one considers the wanton sacrifice of ovaries reported normal by the pathologist. The only justification for a radical attitude is the presence of demonstrable disease in the ovary or the presence of genital cancer when the removal of the ovary is mandatory for obvious reasons.

I like to mention here briefly an observation which has a direct bearing on the difficulties arising over a differential diagnosis between benign and malignant cystadenomas which is in line with the axiom that the only time man is ever really sure is not when he is dealing with scientific matters but when dealing with matters of faith. Unfortunately, faith is not good enough when it comes to making such an important decision as the true nature of an ovarian tumor, yet pathologists, in the final analysis, are forced to rely upon faith. Not being content with this state I have insisted for many years that whenever free fluid is obtainable from the pouch of Douglas it should be studied cytologically, for if it should contain malignant cells it will help immeasurably in arriving at a correct diagnosis and prognosis. The underlying principle was formulated many years ago by the late Ray Watkins, a member of this Society, when he sought information regarding the etiology of endometriosis. I also have made it a practice to study the cytology of intracystic fluids, for they may show malignant components in sufficient numbers to permit a diagnosis when the histologic study of the

specimen does not permit this. With the advent of the Papanicolaou staining method or any of its modifications the study of intraperitoneal and intracystic fluids has become relatively simple.

Dr. Randall's excellent presentation of an old subject proves that there is always more to be learned. To an old-timer it is a joy to learn that the younger generation still considers the ovary worth saving.

DR. RANDALL (Closing).—I would like to thank Dr. Mengert and Dr. Emge for their comments. There are several aspects of this problem we did not consider in the time available. While I feel that leaving one or both ovaries in a woman approaching the menopause preserves her opportunity to develop endometrial carcinoma, even that possibility does not seem to justify taking out both ovaries. Regarding preservation of an ovary·after the menopause, I must confess that I have adopted my present conservative view after, for several years, routinely removing both ovaries when the patient was past 50 years of age. At that time I was impressed by the number of women without periods for years before the operation who, when both ovaries were removed, had very definite exacerbation of their menopausal syndrome. There are several objections to prophylactic bilateral oophorectomy: the dentists say that, if you take out both ovaries, mucous membranes atrophy and dentures no longer fit, while the urologists say the woman with both ovaries removed complains of more dysuria than the woman with some persistence of estrogen effect.

THE MALIGNANCY OF SPECIAL OVARIAN TUMORS*

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SPECIAL ovarian tumors which belong to the dysontogenetic or embryonic carcinoma group are generally considered to be of low-grade clinical malignancy. We have repeatedly encountered exceptions to this generally held opinion and, therefore, have reviewed the clinical histories, follow-up records, and pathologic material of 50 cases. These are made up of 40 cases of granulosa-cell carcinoma,† 7 of dysgerminoma, and 3 of arrhenoblastoma.

Granulosa-Cell Group

The granulosa-cell carcinoma, contrary to other types of malignant ovarian neoplasms, is frequently diagnosed early, before extension through the capsule of the tumor has occurred. This is largely due to the functional activity of the tumor which so often results in uterine bleeding. It may be that early diagnosis rather than low-grade malignancy is responsible for the better 5-year survival rate for these neoplasms than for ovarian carcinoma in general. In any case, early diagnosis presents an opportunity to perform radical surgery when it is most likely to be successful. It was, therefore, disappointing to find that, in 60 per cent of our patients who developed recurrent tumor, treatment had been simple oophorectomy.

The follow-up records of the 40 cases are shown in Tables I to V.

TABLE I. GRANULOSA-CELL CARCINOMA, 40 CASES

Lost	10 cases
Alive and well	15 cases
Recurrences	10 cases
Died from other causes	5 cases
Total	40 cases

TABLE II. DURATION OF FOLLOW-UP IN LOST CASES

1 year	5 cases
2 years	4 cases
4 years	1 case
Total	10 cases

TABLE III. DURATION OF FOLLOW-UP IN PATIENTS DYING FROM OTHER CAUSES

6 months	1 case
2 years	2 cases
7 years	1 case
13 years	1 case
Total	5 cases

TABLE IV. DURATION OF FOLLOW-UP OF WELL PATIENTS

Under 5 years	3 cases
5 years	3 cases
6 to 9 years	5 cases
10 to 15 years	2 cases
15 years +	2 cases
Total	15 cases

A summary of the follow-up records reveals a known recurrence in 10 of the 40 cases, or 25 per cent. When those patients are excluded who were lost to follow-up or died from causes other than recurrent malignancy, in less than 5 years (13 cases), the recurrence rate rises to 35 per cent. Half of the recurrences took place after 5 years and in 2 of these over 10 years had elapsed from the time the primary tumor had been removed. These late recurrences emphasize the value of long follow-up in assessing the malignancy of these tumors.

TABLE V. TIME OF RECURRENCE

Under 5 years	5 cases
5 to 10 years	3 cases
10 years +	2 cases
Total	10 cases

Both the extent of the surgical treatment and the age of the patient influenced the 5-year survival rate. Of the 17 patients who lived 5 years or more, 14 were treated by bilateral oophorectomy and hysterectomy and only 3 by oophorectomy alone. All of the 5 patients who developed recurrence in less than 5 years were treated by oophorectomy. Fortunately, these neoplasms occur with greatest frequency in patients over 35 years of age in whom the preservation of the reproductive function is not of major concern. The influence of age on the survival rate is evident in the 10 patients who developed recurrent tumor. With one exception all were over 39 years. The one exception was that of a 7-year-old child who developed a second granulosa-cell neoplasm in the remaining ovary 6 years after the original oophorectomy. She died 6 years later from undetermined obscure causes which may or may not have been due to recurrent malignancy. The age incidence for all patients is shown in Table VI.

TABLE VI. GRANULOSA-CELL CARCINOMA

Under 10 years	1 case
20-29 years	1 case
30-39 years	5 cases
40-49 years	11 cases
50-59 years	14 cases
60-69 years	5 cases
70 +	3 cases
Total	40 cases

The majority of granulosa-cell carcinomas present a relatively benign histologic appearance. This was true for 7 of the 10 neoplasms which recurred. These were of the follicular, cylindroid or pseudo-adenomatous pattern with the tumor cells exhibiting uniformity in size, shape, and staining qualities. The histologic benign appearance of the neoplasm gave no suggestion of the subsequent malignant course of the disease. In one case a histologically benign cylindroid type of tumor metastasized to the cervix within one year (Figs. 1 and 2), and, in another, a follicular type neoplasm (Fig. 3) did not recur for 11 years. In contrast to this, two histologically malignant tumors have not recurred 9 and 16 years after removal.

It is of interest to note the incidence of multiple primary malignancies in this group of patients. Two patients had previously had carcinoma of the breast 2 and 6 years before the granulosa-cell tumor was removed. One patient developed carcinoma of the sigmoid 13 years after oophorectomy. Two patients had carcinoma of the endometrium and one had carcinoma of the cervix coincident with the granulosa-cell tumor. One of these also had had carcinoma of the breast.
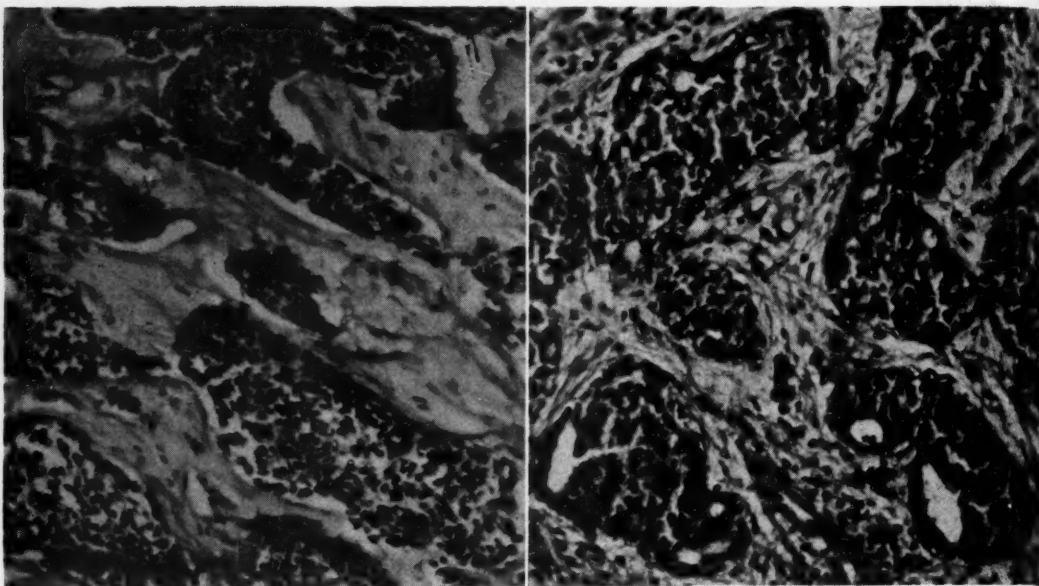
Fig. 1.   Fig. 2.

Fig. 1.—Cylindroid granulosa-cell carcinoma which metastasized to the cervix. (×144.)
Fig. 2.—Secondary granulosa-cell carcinoma of the cervix. Primary tumor shown in Fig. 1.   (×144.)
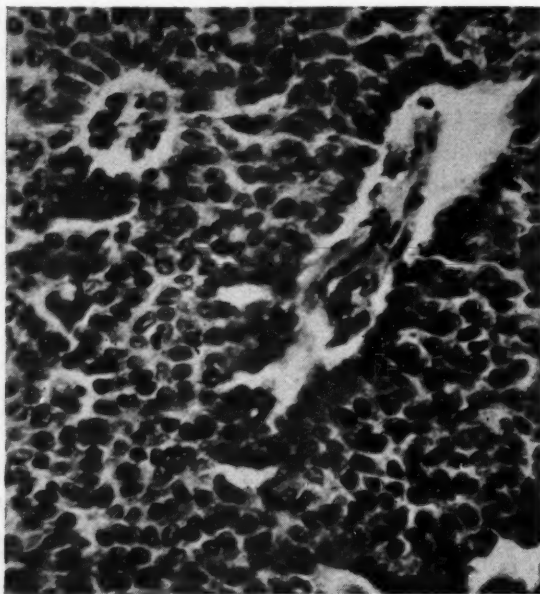

Fig. 3.—Mature follicular type granulosa-cell carcinoma which recurred 11 years after removal.

Our experience has been too limited to reach a definite opinion in regard to the radiosensitivity of these neoplasms. One patient received postoperative high voltage x-ray therapy after supposed incomplete removal of the tumor and has remained well for 13 years. Seven cases of recurrent tumors have been treated. In 6 of these high voltage did not appear to be effective in re-

tarding the progress of the disease. The sixth patient has remained well for one year. The secondary tumor in this case was widely if not completely removed before high voltage was given. The value of routine postoperative high voltage cannot be assessed, but, once recurrence has taken place, in our experience such therapy is unlikely to be effective.

Dysgerminoma

Considerable difference of opinion exists as to the degree of malignancy of these neoplasms. Meyer[2] simply states that many patients remain permanently without recurrence, while Schiller[3] strongly emphasizes the benign nature of the neoplasm in young patients. There is not much statistical evidence, however, to support these opinions as follow-up records of reported cases have been rather inadequate. Dockerty and MacCarty[4] report 2 deaths from recurrent disease in 9 cases. Recently Mueller and associates[5] reported 7 cases and collected information from the literature on an additional 420 cases. From this they note a 5-year survival of 80 patients or 27.3 per cent. They also noted that in 49 cases in which the tumor was unilateral and had an intact capsule, the 5-year survival rate was 89 per cent. The surgical procedures employed in these early cases is not recorded. Our small series of 7 patients further emphasizes the malignant nature of the neoplasm. Five of the 7 patients are dead, and only one has survived over 5 years (Table VII).

TABLE VII

CASES	DURATION	STATUS
2 cases	6 months	dead
1 case	1 year	dead
2 cases	3 years	dead
1 case	1 year	alive and well
1 case	9 years	alive and well
7 cases		

All seven patients were treated by oophorectomy and in only one was there evidence of extension through the capsule of the tumor. In one case, the tumor was bilateral and in one other a second dysgerminoma occurred in the remaining ovary 4 years later.

The tumors were all solid neoplasms, soft in consistency, friable in texture, and exhibited areas of necrosis and hemorrhage. In contrast to many of the granulosa-cell neoplasms and the arrhenoblastomas microscopic diagnosis was not difficult and all tumors presented a remarkably uniform histologic appearance.

These tumors are generally considered very sensitive to high voltage x-ray.[6] Six of our patients received this therapy, 2 are alive and well. Both of these were treated in the immediate postoperative period and in neither was there evidence at operation of extension beyond the capsule of the tumor. Four patients received high voltage treatment after recurrence had taken place and little or no benefit resulted.

TABLE VIII. AGE INCIDENCE OF DYSGERMINOMA

NO. OF CASES	AGE
1	14
1	19
1	28
1	34
1	40
1	45
1	52

Approximately three-fourths of these neoplasms occur between the ages of 10 and 30 years, and it is probable that this early age incidence has influenced the trend of treatment toward conservative surgery. The age of our 7 patients is shown in Table VIII.

Three patients were parous and in one of these the tumor was removed during the puerperium. Despite the rarity of these neoplasms, 11 previous instances of dysgerminoma complicating pregnancy have been reported.[5, 7] One patient was a spinster who had never menstruated and one patient was 52 years of age. In these 5 cases there was little justification for not employing radical surgical treatment.
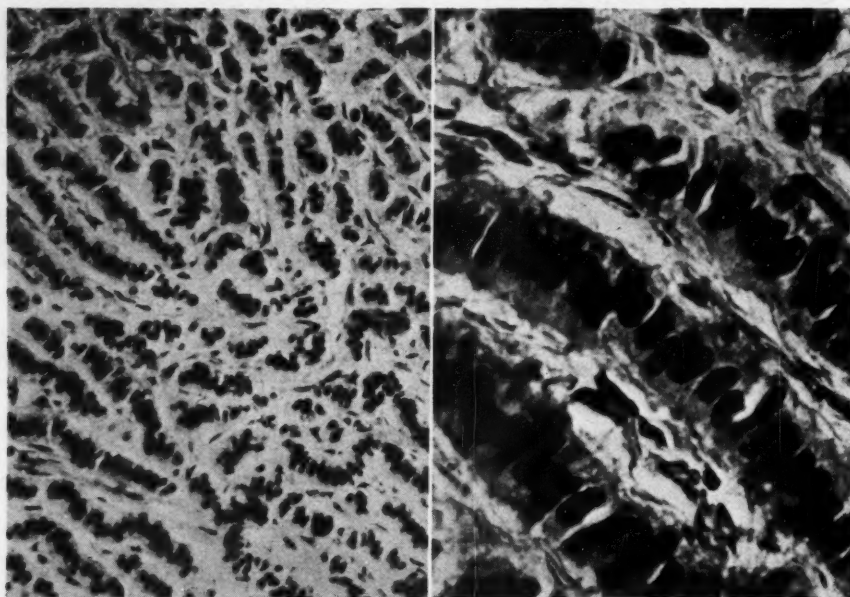

Fig. 4.   Fig. 5.

Fig. 4 (Case 1).—Intermediate type arrhenoblastoma showing long cords of cells with nuclei of the cells lying transversely to the long axis of the column. (×120.)

Fig. 5 (Case 1).—High power of same tumor as shown in Fig. 4. Patient has remained well for 7 years. (×500.)

Arrhenoblastoma

The arrhenoblastoma is the rarest of the three tumors under discussion and their microscopic diagnosis is frequently difficult, particularly in the absence of a clinical history of masculinization. The mature type of tumor, the testicular adenoma of Pick, is readily recognized due to the close resemblance of the tumor tubules to the seminiferous tubules of the testis. The intermediate and sarcomatoid varieties present the greatest difficulties in diagnosis.

Our first case was of the intermediate type and microscopically presented a striking appearance, being made up of long cords of cells with the nuclei arranged parallel to the long axis of the column (Figs. 4 and 5). The patient was 42 years old, had a mild degree of facial hirsutism, and amenorrhea of one year's duration. Treatment was bilateral oophorectomy and hysterectomy. This patient has remained well without evidence of recurrence for 7 years.

The remaining 2 patients were sisters. Each had tumors of similar histologic appearance, being a mixture of the intermediate and sarcomatoid types. A few immature tubules were present, but the most characteristic feature of the

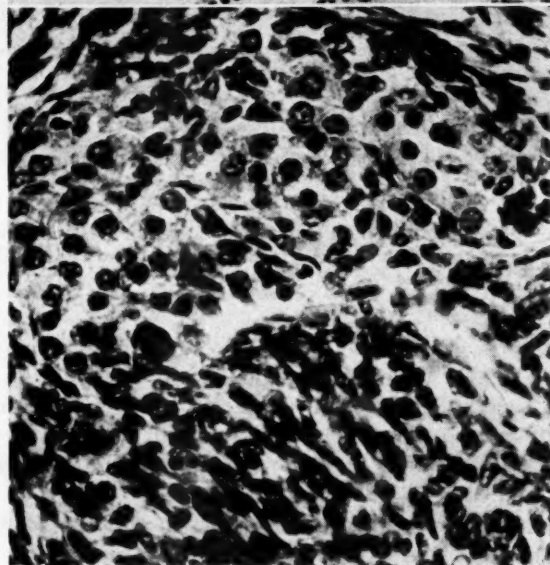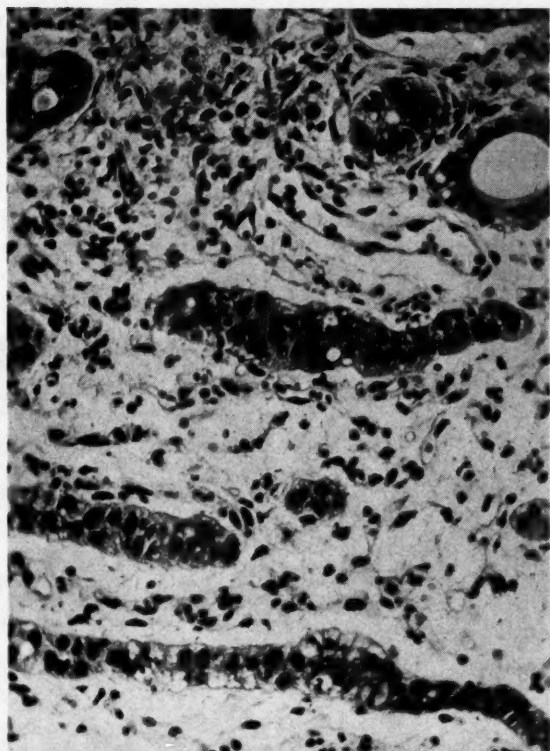Fig. 6.

Fig. 7.

Fig. 6 (Case 2).—Arrhenoblastoma showing cords of cells and immature tubule formation. (×160.)

Fig. 7 (Case 2).—Large mass of interstitial cells. Same tumor as shown in Fig. 6.
Patient died from recurrence in 1 year. (×160.)

neoplasms was the presence in isolated areas of zig-zagging cords of cells and
scattered clumps of interstitial or Leydig type cells, Figs. 6, 7, and 8. Both
girls exhibited similar signs of masculinization, amenorrhea, undeveloped breasts,
mild facial hirsutism, and an adolescent male type of figure. One sister was
19 years of age when the tumor was removed by oophorectomy. This was fol-
lowed by a return of menstruation in 4 weeks. The patient remained well for
only 10 months, when abdominal ascites developed. At laparotomy extensive
carcinomatosis abdominis was encountered. The patient died within one month.
Postmortem examination showed invasion of the peritoneum, omentum, mesen-
teric and retroperitoneal lymph nodes, and liver. The original tumor in this
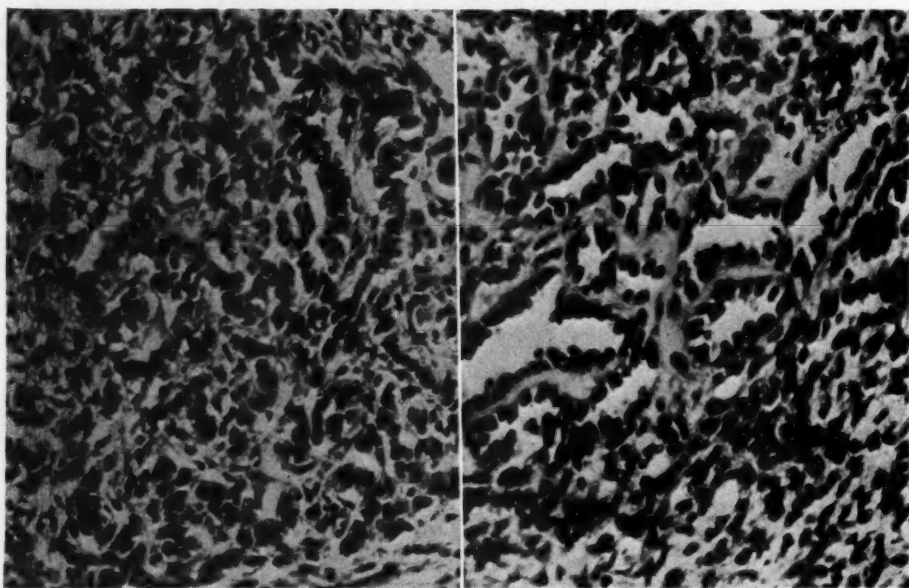case was freely movable. had a long pedicle, and removal appeared to have been
complete.

Fig. 8.   Fig. 9.

Fig. 8 (Case 3).—Arrhenoblastoma showing zigzagging cords of cells. (×120.)
Fig. 9 (Case 3).—Immature tubule formation in same tumor as shown in Fig. 8. Patient
has remained well for 11 years. (×200.)

The second sister was 16 years of age when first operated upon. She
remained well for 4 years when amenorrhea recurred and an abdominal tumor
became evident. At second laparotomy a second arrhenoblastoma of the remain-
ing ovary was removed along with a small infantile uterus. This patient has
remained well for the 11 years since the first laparotomy. At the present time
she is happily married and has adopted children.

The rarity of the arrhenoblastoma has led to the early publication of cases
before sufficient time has elapsed for follow-up. Baldwin and Gafford[8] reported
one case in 1936 and collected 32 cases from the literature, 5 of which had re-
curred. Iverson[9] reviewed the literature again in 1947 and collected 41 more
cases, 6 of which recurred. These added to the 3 cases reported in this paper
bring the total to 78 cases with recurrence and death in 12, or 15 per cent. It
would seem probable that with longer follow-up the incidence of recurrence
would be appreciably higher.

Summary

The clinical course of the granulosa-cell group of neoplasms was extremely varied. Both early and late recurrences took place with histologically benign neoplasms. Half of the recurrences occurred after 5 years. With one exception all patients who developed recurrent tumors were over 39 years of age.

Poorest survival rate was obtained by oophorectomy, whereas 14 of the 17 patients who survived 5 years or longer were treated by bilateral oophorectomy and hysterectomy.

High voltage x-ray therapy for recurrent granulosa-cell carcinoma was ineffective in retarding the progress of the disease.

Despite the apparent favorable extent of the disease in the dysgerminoma group, 5 patients have died from recurrence and only one has survived for 5 years. All patients were treated by oophorectomy.

The rarity of the arrhenoblastoma and the inadequate follow-up records of reported cases make it difficult to estimate the malignancy of this tumor. One patient died of recurrence within a year. One patient developed a second arrhenoblastoma in the remaining ovary in 4 years, but has remained well for 11 years since original oophorectomy. The third patient has survived for 7 years, following bilateral oophorectomy and hysterectomy.

Conclusions

1. The possibility of recurrence of the granulosa-cell carcinoma and the dysgerminoma is sufficiently great to warrant bilateral oophorectomy and hysterectomy for these neoplasms.

2. A known recurrence rate of 15 per cent for the arrhenoblastoma warrants consideration of radical surgery for this rare type of ovarian tumor.

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Discussion

DR. GEORGE H. GARDNER, Chicago, Ill.—Dr. Henderson has made his point, namely, that these tumors are *all* potentially malignant, irrespective of their microscopic appearance. No doubt some of us have been entirely too complacent about them in the past, but I wonder if he isn't unduly pessimistic *now*, and I have misgivings that his advice may lead to unnecessarily radical surgery in the girl, or the young woman, with an encapsulated, freely movable, unilateral tumor.

I have always considered simple oophorectomy as adequate treatment under such conditions. However Dr. Henderson's paper has disturbed my composure on this point; but,

like most others, I have not had sufficient personal experience to justify a strong conviction on these matters. Accordingly we turned to the literature with the hope of gaining further information.

Recently Javert and Finn have followed up as many of the reported arrhenoblastomas as possible, by sending questionnaires to the reporting authors. The total incidence of malignancy in this series was 22 per cent, which is a little higher than usually reported. But it appears to me as pertinent that they found that "malignant" arrhenoblastomas almost always manifested their true nature grossly, either at the operating table, or earlier, by local extension or distant metastases. These authors recommend unilateral salpingo-oophorectomy as adequate treatment for the woman of functional age, with a unilateral, nonextended, freely movable tumor.

Dr. Henderson has referred to a paper on dysgerminomas by Mueller, Tompkins, and Lapp. May I direct your attention again to one of their observations, namely, when the tumor was unilateral, was nonadherent, and had an intact capsule, the five-year survival rate was 89.79 per cent. Unfortunately neither this publication, nor any other, gives data regarding the difference in survival rate after simple removal of such a tumor, in contrast with survival after radical surgery.

The situation in the literature is similar with regard to granulosa-cell tumors. There have been numerous reports on the over-all recurrence rate, which has varied from 8 per cent as found by the Mayo group, up to 31 per cent, as reported by Falls, Ragins, and Goldenberg. Obviously some of these "recurrence" tumors had already extended, or had already metastasized, at the time of surgery; and occasionally one can actually cull this specific information from careful perusal of the text. Yet no one seems to be concerned with the details of the gross findings at surgery, either when discussing mortality statistics or in a consideration of so-called recurrence rates.

Is it not perfectly obvious that we should know the recurrence rate in those patients who had encapsulated, nonadherent, nonextended granulosa-cell tumors of the ovary, before presuming to decide whether simple oophorectomy is relatively safe, or whether radical surgery is always indicated?

One other question seems important. Does the age at which the patient is operated upon influence the recurrence rate? In other words, are granulosa-cell tumors relatively more benign in women of functional age than in those who are postclimacteric? As indicated by Dr. Henderson, this seems to be true. In published reports where these particular data are recorded, few or no recurrences occurred in women who were premenopausal at the time of operation.

In conclusion, may I admit that I am not yet ready to revise my management of these several types of tumors. For the present, at least, I shall consider simple oophorectomy as the preferred treatment for those women of functional age, whose tumors are freely movable and have intact capsules.

DR. EMIL NOVAK, Baltimore, Md.—In the early days of our knowledge of granulosa-cell carcinoma I presented a paper on the subject at the International Congress of Cancer at Atlantic City. In the discussion of my paper, I recall that Dr. Shields Warren, one of our leading pathologists, asked why I spoke of granulosa-cell carcinoma rather than granulosa-cell tumor, since these lesions were all benign. I feel sure that Dr. Warren does not believe this now. It seems to me that the malignant potentialities of this whole group of special tumors have always been somewhat minimized, although even now we are not in a position to speak with any precision about recurrence rates. We are fortunate to have in our laboratory material from approximately 200 granulosa-cell carcinomas, including the 100 or more in the Ovarian Tumor Registry, and also a very large collection of arrhenoblastomas and dysgerminomas. Many of our cases are still within the 5-year limit, and it is becoming increasingly apparent that the follow-up period should be much longer, as recurrence may not appear until after a great many years, especially in the granulosal group. From a rather superficial survey which I have recently made it would seem that something

over 30 per cent of dysgerminomas recur and that the recurrence rate of granulosa-cell carcinoma and arrhenoblastoma is somewhat between 25 and 30 per cent, though these figures are certainly to be looked upon as still quite tentative. Recurrences from granulosa-cell carcinoma have been observed as late as 20 or more years after operation.

The granulosal tumors which occur in very early life are usually diagnosed early because of the rather spectacular biologic manifestations these estrogen-producing tumors produce in this normally estrogen-bare period of life. These symptoms are those of precocious puberty, but it is important to remember that precocious puberty produced by this cause is far less frequent than the so-called constitutional type, in which a perfectly normal puberty mechanism is for some unknown reason released at an abnormally early age, in the absence of any endocrine-producing tumor whatever. In the latter group ovulation and menstruation occur, while ovulation never occurs with the granulosa-cell tumors. It is the constitutional variety, therefore, which is responsible for the numerous reported cases of abnormally early motherhood, such as the case of the little Peruvian girl, Lina Medina, the youngest mother in the history of the world.

The moral is that one should refrain from operating upon patients with precocious puberty if pelvic examination, usually under anesthesia, reveals no enlargement of either ovary. As regards arrhenoblastoma, the mere existence of such symptoms as hirsutism, flat breasts, and amenorrhea, plus a unilateral pelvic tumor, does not justify the diagnosis of arrhenoblastoma if, as is so often the case, these symptoms date from early life, since under these circumstances the intersexual manifestations are generally of genetic origin, and the tumor of the ovary is a purely coincidental one, such as an ordinary cystadenoma. The presumption of masculinizing tumors is far stronger when a tumor is found in a woman who develops such symptoms rather abruptly against a previously normal feminine background. The most important aspect of these tumors pertains to their pathology and histogenesis, but there is not time to go into this.

DR. DANIEL G. MORTON, Los Angeles, Calif.—Recently I had an opportunity to observe a patient who had a dysgerminoma whose course was very remarkable to me and I thought it might be interesting to you. I would like to report it very briefly.

The patient was a young 18-year-old unmarried nulligravida whose past history was quite normal: normal physical development, normal sex history, and normal menstrual history. In 1946, when she was eighteen years old, she began to have enlargement of the lower abdomen and this increased rapidly. She saw a doctor whose only treatment was to take a pregnancy test. This proved negative and nothing was done for four months, during which time she was simply observed. In January, 1947, she was operated upon and at that time a large tumor was found in the pelvis involving the right ovary and uterus and described as a fibrous mass. This was removed, including both tubes, the right ovary, and the uterus; the left ovary appeared normal and was not removed. The pathologic diagnosis was dysgerminoma; there was no evidence of metastasis and nothing further was done. Ten months later the patient had pain in the right lower quadrant, backache, constipation, fever, and vomiting. She grew rapidly worse and was almost moribund. She was operated upon and the surgeon found an inoperable growth in the pelvis. Biopsy was taken of the liver which turned out to show cirrhosis only. As a desperate measure the patient was given nitrogen mustard over the period of the next four days, 5 mg. a day, with a very dramatic result. On the fifth day she was up and about and had started to eat again, and on the eighth or ninth day she walked out of the hospital apparently well. She came back again on several occasions with recurrences of somewhat similar nature. There were four readmissions during the course of the next three years with symptoms and signs of similar character; on each occasion nitrogen mustard was given and on each occasion she responded remarkably, was able to go to work in the intervals between attacks, was robust, and even rode a motorcycle to work. However, in April, 1951, four and one-half years after the beginning of the illness, she died and postmortem examination revealed widespread metastases which microscopically were identical with the original tumor. Since few of us have heard of response of such a tumor to nitrogen mustard, I thought you might like to have this case report.

DR. HENDERSON (Closing).—It was an unfortunate time to arise and advocate radical surgery on the ovary after Dr. Randall's plea to conserve this organ. The fact remains, so far as our cases of arrhenoblastoma are concerned, that the two patients who are alive and well had both ovaries and the uterus removed, one at the original time and the other for a recurrent tumor in the remaining ovary, six years later. I think any lesion which, according to the information we have available in the literature, has a likelihood of recurrence and a death rate as high as 15 per cent, does warrant consideration of radical surgery. So far as our cases of dysgerminoma are concerned, it would have been no great sacrifice to perform a bilateral oophorectomy in five cases and certainly we could not have had worse results.

Dr. Gardner has suggested that we do not know what happens to patients with granulosa-cell neoplasms which have, in the gross, not extended beyond the capsule of the ovaries. That is true. They have not been followed up for a long enough time. The course of the granulosa-cell neoplasm is not predictable. When we reviewed our cases nine years ago, the recurrence rate was 14 per cent, and today it is 25 per cent, and in those adequately followed it is 35 per cent. All those recurrences occurred in women over 39 years of age and, in the five patients who developed recurrence after five years, all had freely movable neoplasms with apparent intact capsules.

Ovarian malignancy carries with it such a high mortality rate that where the opportunity presents itself for radical surgery before there is an extension beyond the capsule of the tumor, it would appear to me that it is an opportunity that should be accepted.

EXCRETION AND CONCENTRATION OF URINE SOLUTES DURING NORMAL PREGNANCY AS MEASURED BY FREEZING POINT DEPRESSION[*][†]

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THE purpose of this study was to determine whether normal pregnancy altered the renal excretion of urinary solids. Ostetricians frequently express the opinion that pregnancy is the best test of renal function. Statements may be found in textbooks that pregnancy imposes a "load" on the kidneys and that the excretion of waste products increases as pregnancy advances. Studies to support these opinions are not found in the literature.

The renal function tests which have been used in an attempt to ascertain the effect of pregnancy on the kidney have given variable and conflicting results. Urea clearance,[1, 2, 3] the urea concentration test,[4] and the phenolsulfonphthalein excretion test[2] are all essentially normal during uncomplicated pregnancy. Likewise the effective renal blood flow, filtration rate, and total functioning tubular mass are unchanged by normal pregnancy and delivery.[5, 6, 7] However, the concentration and dilution test reveals some inability on the part of the normal pregnant patient to concentrate the urine.[8] A study of the urinary sediment has been used as a function test in normal pregnancy.[9] Addis counts disclose a marked increase in formed elements in the urine during the last trimester. This is interpreted to be the result of physiological dilatation of the ureters rather than from pathological changes.[10] On the basis of their studies, Theobald and Verney concluded that posture played a role in influencing urine volume. They felt that the upright position produced mechanical pressure which impeded venous return from the legs and thus made less fluid available for excretion by the kidneys.[11]

Renal Function

In a broad sense renal function consists of the glomerular filtration of plasma and the tubular reabsorption of a large part of the filtrate. The purpose of this function is the concentration and excretion of solutes, the transport and excretion of water, and to act as an adjunct to the acid-base regulation of the body fluids.[12]

Filtration is the result of physical energy supplied by the heart, whereas tubular reabsorption is the result of active work by the kidneys. Renal adjustment of body water and the chemical pattern of the blood necessitate the production of a solution that differs in many respects from plasma (Fig. 1).[13] Urine, the solution which is the end result of this regulatory mechanism, is constructed by a selective reabsorption of the filtrate as it passes through the tubules. In the glomerular capsule the filtrate is chemically identical with plasma except for the absence of certain proteins and lipids in the former.

The greater part of the water and most of the solids are reabsorbed in the proximal tubules. Water and osmotically active solids are reabsorbed in such proportions that the filtrate reaching the distal tubules has a molecular concentration approximately that of plasma.[14] Some doubt exists as to whether the transfer of filtrate through the proximal tubular epithelium requires energy.[14, 15] As a result of reabsorption of both water and sodium in the proximal tubule a sharp osmotic gradient does not occur between filtrate and plasma. The lack of this over-all concentration difference suggests that the process of transfer is not attained through the expenditure of osmotic energy. However, if energy is required in order to transfer molecules through cells the energy must be supplied by chemical reactions occurring in the cells of the tubular epithelium.

Fig. 1.—Normal blood plasma and urinary constituents. (From Gamble.[15])

In the distal tubules selective reabsorption of water and electrolyte occurs. If the body demand is for water rather than electrolytes more water will be reabsorbed into the plasma and the osmotic pressure of the filtrate increases. The construction of a concentrated urine ceases when the tubular epithelium is no longer able to overcome the increasing osmotic resistance offered by the filtrate. In contrast to the chemical energy expended in the proximal tubules, the process of reabsorption in the distal tubules is the result of the expenditure of osmotic energy.

When excess water is available to the nephron for excretion of metabolic products, dilute urines are excreted. In the normal pregnant state the decrease in total base requires that maximum amounts of sodium be reabsorbed from the filtrate. Therefore, if ionic equilibrium is to be maintained, the tubular filtrate must be more completely cleared of the sodium ion. This requirement is increased when low-sodium diets are used.

Principle of Freezing Point Determination

Urine is a solution of solutes dissolved in water (Fig. 1). The osmotic pressure of a solution is directly proportional to the molecular concentration. Molecular concentration and osmotic pressure of solutions may be measured in several ways, most of which are technically difficult. Findlay[16] (1905) described freezing point depression as a practical means for determining the molecular concentration of body fluids. Recent advances in physical chemical methods have made freezing point determinations simple, practical, and well within the ability of any trained technician.

If the freezing point depression of the solution is determined, the molecular concentration may be calculated. The basis for the calculation is as follows: a gram mol (1,000 milliosmoles) of any solute in solution produces a freezing point depression of $-1.86°$ C. Dividing the freezing point depression of the given solution by 1.86 gives concentration in osmoles per liter or milliosmoles per cubic centimeter. Multiplying the milliosmole concentration by cubic centimeters of solution gives a measurement of total solutes in the solution. Thus the total output and concentration of substances excreted by the kidney over a unit of time can be readily determined.[16]

Example: 24-hour urine volume = 1240 c.c.
Freezing point depression $-1.19°$ C.
1.19/1.86 = 0.64 osmole/1 or milliosmoles/c.c.
1240 × 0.64 = 794 milliosmoles = total solute output/24 hr.

Method and Material

The cryoscope which is used to determine the water content of milk can be easily modified to measure accurately the freezing point depression of urine solutions. When the standard cryoscope thermometer is replaced by a Beckmann thermometer, accurate and reproducible results are obtained. In this study the Beckmann thermometer was calibrated against distilled water and sucrose solutions. All freezing point depression determinations of the urine samples were done in duplicate. The determination of total urinary nitrogen has been completed in all but a few specimens.

Twelve healthy primiparas and multiparas were the subjects for the study. Ten had uneventful pregnancies, uncomplicated deliveries and afebrile puerpera. Two patients of this group had twin pregnancies. All patients in the group were unrestricted as to diet and fluid intake. The usual prenatal suggestions were given but no effort was made to limit the patients' dietary regimen or activities in any manner.

One hundred ninety-three 24-hour specimens of urine were studied, and they are the basis for this report. The earliest determination was made 203 days prior to delivery and several urine specimens were collected the day prior to the onset of labor. The postpartum values determined 5 to 29 weeks after delivery are considered to represent the nonpregnant values for these individuals.

TABLE I.   TWENTY-FOUR HOUR URINE VOLUMES, TOTAL SOLUTES, SOLUTE CONCENTRATION, AND TOTAL NITROGEN DURING PREGNANCY

| PATIENT | WEEK | | URINE VOL. C.C./24 HR. | TOTAL SOLUTES | | URINE N. GM./24 HR. |
	ANTE-PARTUM	POST-PARTUM		MOS./24 HR.	MOS./C.C.	
1	23		1,675	831	0.496	
	24		1,310	700	0.535	
	25		1,560	772	0.495	
	26		1,500	819	0.545	
	27		1,370	1,002	0.745	9.5
	28		1,130	873	0.770	8.4
	29		1,630	1,067	0.655	10.1
	30		1,150	878	0.763	7.9
	31		1,430	952	0.665	8.7
	32		1,810	1,192	0.660	7.4
	33		1,820	983	0.540	9.7
	33		1,710	785	0.460	9.8
	34		1,430	1,076	0.753	9.2
	34		1,760	778	0.442	8.5
	35		1,375	1,006	0.771	8.3
	36		1,660	945	0.570	
	37		1,880	889	0.464	8.1
	38		2,070	1,136	0.550	9.1
	38		1,820	1,173	0.645	10.6
	39		1,560	971	0.623	11.6
	39		1,470	808	0.550	8.0
	40		1,340	792	0.590	7.6
		26	1,140	693	0.608	8.7
		27	1,160	870	0.750	9.3
		28	1,120	797	0.710	10.8
		29	1,670	991	0.594	11.6
2	25		1,570	1,158	0.736	
	26		1,680	1,444	0.861	9.6
	29		1,770	1,430	0.809	13.3
	29		1,920	1,365	0.710	13.5
	30		1,290	1,377	1.060	12.4
	32		1,510	1,461	0.970	16.6
	32		1,380	1,212	0.880	10.5
	33		1,710	1,620	0.950	16.1
	34		1,440	1,272	0.885	13.8
	36		1,710	1,397	0.817	13.2
	36		1,590	1,265	0.795	13.4
	37		1,620	1,263	0.780	16.9
	38		1,555	1,186	0.764	12.6
	39		1,190	895	0.750	10.5
	40		1,700	1,318	0.775	13.6
		21	725	896	1.230	11.5
		22	1,075	997	0.930	12.7
		24	1,295	1,318	1.000	17.7
		25	1,040	1,053	1.000	
3	19		1,400	790	0.564	
	20		1,450	865	0.595	
	21		1,430	1,116	0.780	8.9
	22		1,870	1,525	0.815	10.7
	23		1,590	1,420	0.894	10.7
	24		1,835	1,137	0.620	12.1
	25		1,510	1,281	0.850	11.9
	26		1,460	1,256	0.860	12.0
	29		1,290	1,430	1.110	13.2
	30		1,140	1,104	0.970	9.4
	31		1,270	1,176	0.926	8.0
	32		810	835	1.030	8.6
	33		1,760	966	0.550	10.1
	34		1,410	1,184	0.840	12.4
	35		1,170	906	0.770	8.4
	37		1,318	1,077	0.819	8.0

TABLE I—CONT'D

PATIENT	WEEK		URINE VOL. C.C./24 HR.	TOTAL SOLUTES		URINE N. GM./24 HR.
	ANTE-PARTUM	POST-PARTUM		MOS./24 HR.	MOS./C.C.	
		18	1,037	872	0.840	9.4
		20	980	829	0.846	
		21	965	595	0.617	
4	33		1,510	1,007	0.710	8.8
	34				0.645	
	35		1,350	871	0.645	8.9
	35		1,870	924	0.494	10.5
	36		2,030	806	0.396	7.5
	37		2,290	1,231	0.540	10.8
	37		2,110	1,157	0.548	13.2
	38		1,110	705	0.635	9.3
	39		1,360	905	0.665	9.0
		22	1,725	821	0.477	9.7
		24	1,590	1,030	0.648	11.8
		24	1,415	925	0.654	11.7
		25	1,880	929	0.495	
5	32		1,500	1,050	0.700	10.1
	33		815	571	0.700	6.3
	34		1,760	1,073	0.610	10.6
	35		1,200	660	0.550	6.9
	36		1,550	884	0.570	10.4
	37		1,110	766	0.690	7.8
	37		1,430	786	0.550	8.9
	38		1,365	915	0.670	11.0
	38		2,080	1,165	0.560	11.4
	39		1,650	1,106	0.670	11.9
	40		2,000	1,000	0.500	11.0
6	21		600	526	0.860	
	23		600	444	0.740	
	27		610	420	0.690	
	28		640	576	0.900	
	29		730	581	0.795	4.6
	30		730	630	0.861	6.1
	31		655	534	0.816	3.7
	32		980	706	0.720	7.9
	33		1,050	756	0.720	8.6
	34		530	530	1.000	4.7
	35		540	516	0.955	3.9
	35		741	736	0.993	7.7
	36		1,070	874	0.815	7.2
	37		530	615	1.160	6.4
	38		270	267	0.990	3.1
	38		545	602	1.100	5.8
	39		450	373	0.830	3.9
		23	1,020	664	1.020	7.4
		24	730	614	0.730	8.9
		25	883	860	0.880	11.6
		26	690	490	0.690	
7	28		1,250	737	0.590	
	30		1,395	1,019	0.730	
	31		1,635	752	0.460	
	32		1,160	800	0.690	
	34		1,000	690	0.690	
8	11		1,110	1,160	1.040	9.4
	12		960	1,050	1.100	10.7
	13		900	1,087	1.200	9.5
	14		1,510	1,220	0.810	12.4
	15		1,115	982	0.880	7.9
	17		1,230	1,032	0.840	10.1
	18		1,280	1,018	0.845	11.3

TABLE I—CONT'D

| PATIENT | WEEK | | URINE VOL. C.C./24 HR. | TOTAL SOLUTES | | URINE N. GM./24 HR. |
	ANTE-PARTUM	POST-PARTUM		MOS./24 HR.	MOS./C.C.	
	19		1,375	1,153	0.840	12.1
	21		1,200	1,070	0.890	10.7
	24		840	795	0.947	10.1
	25		1,210	884	0.730	10.1
		5	930	658	0.710	7.4
		6	1,240	831	0.670	9.7
		7	880	855	0.972	11.5
		8	850	791	0.930	9.9
9	25		870	618	0.710	8.0
	28		1,080	885	0.820	
	29		1,030	639	0.620	
	30		1,215	839	0.690	
	31		1,260	680	0.540	
	32		850	697	0.820	
	33		1,345	808	0.600	
	34		1,580	806	0.510	8.1
	35		1,075	785	0.730	9.2
	36		1,225	884	0.720	9.5
	37		765	619	0.810	8.4
	39		1,000	620	0.620	
10	33		1,735	764	0.440	
	34		1,800	738	0.410	
	35		1,710	719	0.420	
	36		1,745			
	37		1,735	729	0.420	
	38		1,625	715	0.440	
	39		1,580	726	0.460	
11	28		1,710	889	0.520	
	29		2,450	956	0.390	
	29		2,400	890	0.370	10.3
	30		3,283	1,313	0.400	15.5
	31		2,665	1,145	0.430	13.6
	32		2,645	1,137	0.430	11.1
	33		1,975	830	0.420	9.0
	34		2,050	861	0.420	10.8
	36		3,030	848	0.280	10.7
	37		2,810	872	0.310	
	38		3,300	1,122	0.340	
12	30		1,145	801	0.700	
	30		1,400	925	0.660	
	32		1,310	930	0.710	
	33		1,625	829	0.510	
	35		1,160	696	0.600	
	36		1,390	792	0.570	
	37		765	581	0.760	
	37		1,830	800	0.470	
	38		700	497	0.710	
	38		1,300	794	0.610	
	39		1,125	630	0.560	

Results

The results obtained when the daily total urinary solutes were determined in this group are illustrated in Fig. 2. The excretion of solutes by the individual patients are seen in Table I. The total solute excretion ranged from 300 to 1,600 milliosmoles for the group. However, the individual patient showed a variation of approximately 200 milliosmoles from her mean solute output.

Illustrated graphically in Fig. 3 are the solute concentrations per cubic centimeter of urine for each of these women in a 24-hour period. Also illus-

trated is the mean milliosmolar concentration for the group. The osmolar concentration of plasma during the latter part of pregnancy is 0.28. The most dilute urine collected was one and one-half times more concentrated than plasma. The average osmolar concentration for the group is almost two and one-half times that of plasma. Individual variations in solute concentration were from 0.2 to 0.5 milliosmole per cubic centimeter of urine as shown in Table I.
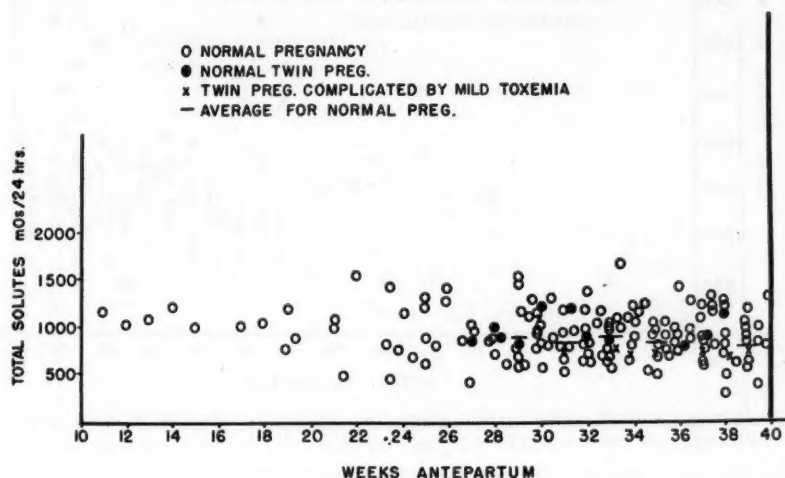

Fig. 2.—Urinary solutes, milliosmoles per 24 hours, during normal pregnancy.

Fig. 3.—Urine solute, concentration, milliosmoles per cubic centimeter, during normal pregnancy.

Fig. 4 illustrates the individual and mean urine volumes for 24-hour periods. This chart represents the residual water which is present after facultative and obligatory reabsorption and is available for the excretion of the solute mass. Daily urine volumes seldom varied more than 400 c.c. in individual patients, and the average volumes for the group revealed no trend in either direction. Certainly, there was no evidence of a decrease in urine volume during the last trimester.

Fig. 5 illustrates the economy of the kidneys in handling different solute masses. It is noted that during pregnancy the solute excretion is within the

ranges of maximum renal economy. The mean urine volume of this group was 1,350 c.c. per 24 hours and the mean solute concentration was 0.7 milliosmole per cubic centimeter.
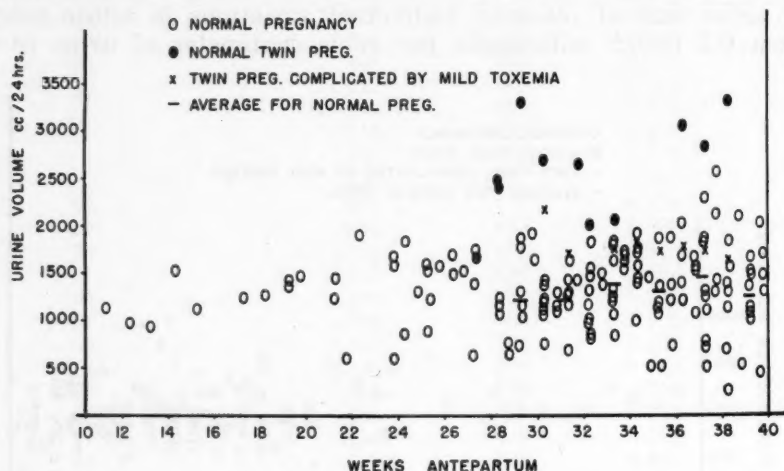

Fig. 4.—Urine volume, cubic centimeters per 24 hours, during normal pregnancy.
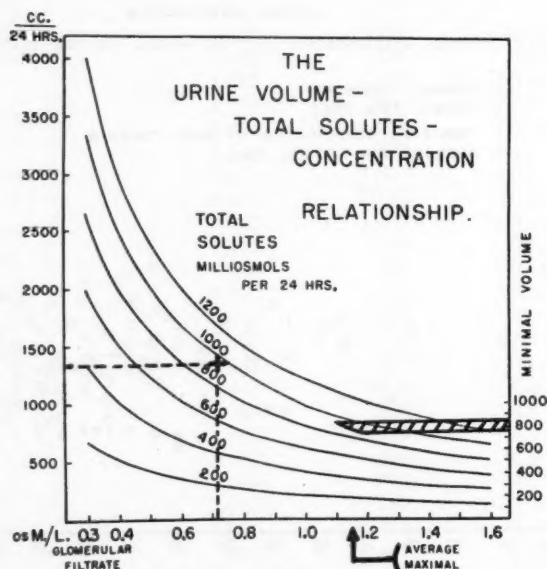

Fig. 5.—Illustrates the urine volume-total solute concentration relationship: X is the average relationship during normal pregnancy as determined in this study. The hatched area describes the minimal urine volume that is required to remove this load during pregnancy. Urine volume below this minimal requirement defines oliguria. (From Gamble.[13])

Fig. 6 illustrates the individual and average excretion of nitrogen. During gestation, no significant variation in total nitrogen excretion is evident. These findings are consistent with the solute excretion pattern described above and do not materially differ from the results of previous investigative work. Twenty-four hour creatinine excretions completed in one-half of the patients averaged 1,100 mg. There was no change in excretion as pregnancy advanced (Fig. 7).

In an effort to determine the maximal ability of the kidney to concentrate solutes, a rather marked fluid restriction was imposed upon several young, healthy primiparas in the last trimester of pregnancy who were hospitalized but ambulatory. During a thirty-six hour period total fluid was limited to 500 c.c. This included both the water of food and the liquids drunk. At the end of 36 and 38 hours of dehydration, specimens of urine were collected. The
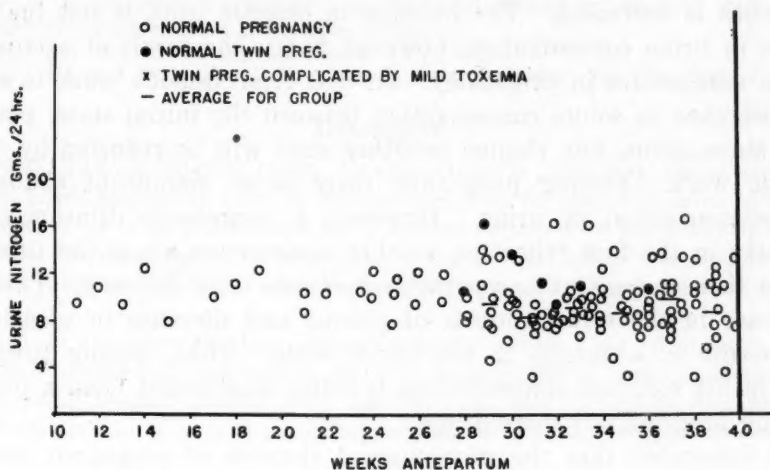

Fig. 6.—Total urine nitrogen, grams per 24 hours, during normal pregnancy.
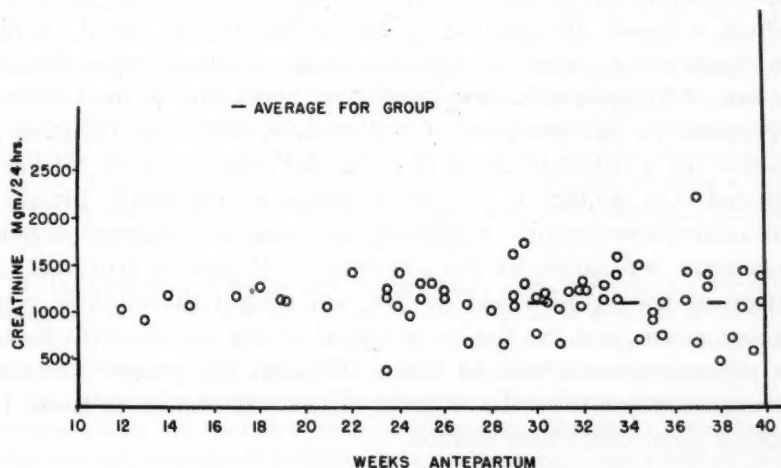

Fig. 7.—Creatinine excretion, milligrams per 24 hours, during normal pregnancy.

average molecular concentration of these urine specimens was from 1.1 to 1.2 milliosmoles per cubic centimeter. The average maximal concentrating ability for the male is 1.4 milliosmoles per cubic centimeter.[17] The concentrating ability of normal nonpregnant women varies between 1.1 to 1.3 milliosmoles per cubic centimeter. Several pregnant patients with known renal disease were subjected to the same dehydration procedure. These patients were never able to concentrate above 0.85 milliosmole per cubic centimeter of urine even on subsequent attempts.

Comment and Conclusions

The results of this study show that the excretion of waste products by the kidney is not increased during normal pregnancy as denoted by the quantity of total solutes appearing in the urine. It is interesting to note that the total solute excretion does not increase in spite of an increase in maternal mass and the presence of a growing fetus. However, the results do suggest that renal osmotic work is increased. The increase in osmotic work is not the result of variations in urine concentration, however, but is the result of a true dilution of plasma that occurs in pregnancy. In that renal osmotic work is a function of the difference in solute concentration between the initial state, plasma, and the final state, urine, any change in either state will be reflected by variations in osmotic work. During pregnancy there is no significant change in the osmolar concentration of urine. However, a progressive dilution of plasma occurs early in the first trimester, reaches a maximum about the thirty-second week, and then concentration gradually increases until delivery. This progressive increase in the water content of plasma and decrease in plasma concentration results in a change in the initial state. Thus, during pregnancy, a urine of rather constant concentration is being constructed from a plasma that is becoming progressively more dilute.

It is concluded that the physiological changes of pregnancy produce an increased osmotic pressure difference between the tubular filtrate and the plasma. The formation of urine in the presence of this increased osmotic gradient requires the expenditure of more osmotic energy. The freezing point depression method offers a means for evaluating the ability of the distal tubule of the kidney to construct a urine of optimum and maximum concentration. The determination of urine specific gravity during pregnancy is inadequate for this purpose because, in the presence of proteinuria, the large albumin molecule does not allow for a true estimation of molecular concentration. It has recently been suggested that damage to the distal tubule is responsible for the oliguria of the pre-eclamptic-eclamptic syndrome and also the oliguria accompanying severe premature separation of the placenta.[18] If this be true, the molecular concentration of the urine would be low, but should the oliguria result from an extrarenal cause such as the presence of excess antidiuretic hormone the molecular concentration would be high. Finally, the progressive changes in tubular function associated with oliguria of toxemia can be followed by means of the freezing point depression method.

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Discussion

DR. WILLIAM J. DIECKMANN, Chicago, Ill.—Dr. Reid and his co-workers have done a tremendous amount of work on the freezing point depression of urine in these pregnant patients. This is an old method and I am not certain why Dr. Reid has revived it. I have studied the report and the tables but he has not sold me on this method for determining renal function. Perhaps when he has more cases he can substantiate some of his claims.

The kidney has many functions and whenever it has been cut off abruptly, as occurs with bilateral ligation of both ureters or with so-called lower nephron nephrosis, these various functions become obvious very quickly. Dr. Reid mentioned the hemodilution which is characteristic of normal pregnancy and stated that it caused additional work by the kidney.

Dr. Reid stated that the antepartum values based on freezing point determinations did not show increased excretions of total solutes during pregnancy, but when I look over his table my impression is that most of the patients for whom both antepartum and postpartum values were given showed an increased excretion during pregnancy. The kidney has to excrete urea and nonvolatile acids and bases in addition to water. The urea content of the urine depends primarily on the protein intake. I wonder if Dr. Reid has paid any attention to urea, which will affect the freezing point depression. The nitrogen intake, according to his figures, ranges from 4 to 16 Gm. per day, which is a tremendous variation and would result in marked variations in freezing point determinations. I believe the study would be of more significance if the patients were studied while on a constant diet with controlled fluid intake, determinations of urea, nonprotein nitrogen, and electrolytes, and preferably a constant temperature and humidity.

DR. REID (Closing).—I would like to thank Dr. Dieckmann for his discussion. True, this is a reintroduction of an old method but modified so as to make it of practical clinical use. The total amount of solutes excreted in twenty-four hours by these patients did vary in amount. However, the individual patient failed to show any increase in the total solutes as the pregnancy progressed. Furthermore, creatinine determinations (Fig. 7) revealed values which also did not vary as pregnancy advanced, furnishing additional evidence that the solutes did not increase during this period. There was no evidence that the fetal mass as it increased in size contributed to the total solutes excreted. Thus, the differences seen in total output are dependent on the size of the individual and reflect the amount of food eaten.

The idea has been revived that tubular damage is an important pathological change in the kidneys of the severely toxemic patient, accountable for the subsequent oliguria and anuria. We believe that this method will afford an opportunity to determine the validity of such a concept. Freezing point depression will furnish an index of the amount of tubular damage and the recovery of tubular function may be followed.

COMPLETE CESAREAN HYSTERECTOMY*

A Logical Advance in Modern Obstetric Surgery

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THE pattern of obstetric care in the United States has changed materially in recent years. Maternal mortality has been reduced spectacularly by a number of factors. Some of these are the increasing hospitalization of women for delivery, greater safety of pregnancy and parturition as a result of many outstanding developments in medical and obstetric practice, improved physical facilities, and better trained personnel who have waged a relentless war against the hazards of childbirth. Each year has witnessed a progressive decrease in mortality rate. At the mid-century the national figure of less than one per thousand live births made a real impression on all of us. Indeed, in most large maternity hospitals and teaching centers a mortality figure of no more than one-third the national average has been attained.

The role of abdominal delivery has been important in this remarkable improvement in obstetric practice. The increased safety of cesarean section has resulted in a re-evaluation of the indications for its use. Thus, difficult and traumatic delivery from below has been replaced by abdominal delivery. The hemorrhagic complications of late pregnancy are managed more adequately and more safely by cesarean section. No longer is cephalopelvic disproportion the major cause of difficult labor. Serious failures in the labor mechanism may serve equally well to obstruct otherwise normal parturition. Delivery through the natural passages is still the most desirable goal, for it is safe and physiologic, but it is no longer desirable at any price. We have all witnessed the tragic sequelae of such a policy.

However, in many institutions the increased safety of cesarean section and the realistic appraisal of its modern role in obstetrics have not necessarily resulted in a greater use of this mode of delivery. Experience of two decades at the Chicago Lying-in Hospital has not brought with it an increased incidence. It has remained at about 5 per cent (Table I). Thus, with more experience we have selected patients for cesarean section more intelligently, broadening the indications without increasing the frequency of the procedure.

The Chicago Lying-in Hospital has pioneered the development of the low or cervical cesarean section. Its advantages over the classical operation for patients in labor have been proved by 25 years of experience. Although the advantages of laparotrachelotomy for patients not in labor may be less dramatic, it is the operation of choice for the individual who is a competent surgeon.

During the last 20 years there has been an increasing interest in our clinic in cesarean hysterectomy, reflected in the increasing frequency of the operation. In the past, the removal of the uterus following delivery was carried out primarily for disease, rarely to reduce the hazard of peritonitis in patients potentially or obviously infected, and occasionally as a means of preventing further childbearing in women late in the reproductive lifetime.

TABLE I. CESAREAN SECTIONS, CHICAGO LYING-IN HOSPITAL, 1931-1951

DATES	5/31-9/34	9/34-3/38	3/38-3/42	3/42-7/48	7/48-4/51
Number	500	500	500	983	736
Incidence	5.6%	5.5%	4.4%	5.1%	5%
Laparotrachelotomy	92%	93%	91%	89%	71%
Cesarean hysterectomy	6%	6%	7%	9%	19%
Maternal mortality					
Number	5	3	2	1	1
Per cent	1.0%	0.6%	0.4%	0.08%	0.13%

Prior to 1947 cesarean hysterectomy consisted of the removal of the uterus at a high level, leaving all of the cervix and often portions of the uterus. These high amputations were regarded as expedient because of the increased vascularity of all the structures during late pregnancy and the greater hazard of bladder and ureteral damage during surgery. Quite often the large cervical stump gave rise to symptoms. In the multigravida poor support allowed it to prolapse and cause discomfort. It was subject to infection, erosion, and malignant change. It became painful and caused dyspareunia. Occasionally bleeding occurred and it was necessary to rule out malignant disease. Many cervical stumps had to be removed later in life. Thus, the same arguments which justified the trend in gynecologic surgery toward complete removal of the uterus can be mustered in defense of the removal of the entire uterus at cesarean section.

Material

Since July 1, 1947, we have delivered 14,749 mothers at the Chicago Lying-in Hospital, 736 of these by the abdominal route. The low or cervical cesarean section was performed on 596 women. Forty women had incomplete and 100 complete cesarean hysterectomies (Table II). One mother who had a laparotrachelotomy died on the ninth day following sudden pulmonary embolism. All of the women who had cesarean hysterectomies made good recoveries.

Indications

The removal of the uterus following cesarean section is justified only if certain conditions are present: in the first place, if the termination of childbearing because of medical indications has been decided upon by the physician and the family; second, if the uterus is abnormal because of neoplasms, gross scarring from previous sections, disease or extensive trauma of the cervix, or other pathologic conditions; third, in women near the end of their reproductive period, in whom the uterus no longer serves a useful function; last, the operation must not result in increased morbidity or mortality, and it must provide favorable physiologic conditions for normal sex life.

Our indications for cesarean hysterectomy are listed in Table III. It will be noted that half of the women had one or more previous cesarean operations. In many of these patients the termination of the reproductive function was

only one factor which influenced the decision to remove the uterus. It has been the policy of our clinic to do an elective abdominal delivery a week or so before term in most mothers who have had a previous cesarean section. This age-old practice, "once a cesarean always a cesarean," has been subject to considerable discussion of late. There is a rising tide of opinion favoring delivery from below for many of these women with uterine scars. That such a course is feasible in many of them is certain. However, so little is to be gained by a successful delivery through the natural passages that it rarely compensates for the hazard of uterine rupture, though it may be small. Furthermore, a successful delivery from below following a previous cesarean does not necessarily guarantee the integrity of the scar in future pregnancies, yet such an accomplishment does give to the patient a false sense of security. Indeed, the hazard of elective cesarean section is so small today that the results in many thousands of cases will have to be compiled to prove that our time-honored practice can now be ignored.

TABLE II. CESAREAN SECTIONS, JULY 1, 1947, TO APRIL 1, 1951

	NUMBER	PER CENT	INCIDENCE	MORTALITY
Laparotrachelotomy	596	81		0.17%*
Cesarean hysterectomy		19		
Incomplete	40			0
Complete	100			0
Total	736	100	5%	0.13%

*Cesarean section death from embolism, August, 1948.

TABLE III. INDICATIONS* FOR CESAREAN HYSTERECTOMY, JULY 1, 1947, TO APRIL 1, 1951

	COMPLETE	INCOMPLETE
Previous cesarean section	50	21
One section	36	11
Two sections	12	7
Three sections	1	3
Four sections	1	0
Leiomyomas of uterus	26	10
Disease of cervix	10	3
Placenta previa	9	1
Abruptio placentae	1	0
Chronic hypertensive disease	7	5
Diabetes	8	7
Cardiac disease	8	3
Incomplete uterine rupture	2	0
Carcinoma rectum	1	0
Leucemia	1	0
Huge ventral hernia	1	0
Over 40 years old	15	6

*More than one indication in the majority of patients.

About one of every four uteri in our series exhibited leiomyomas of appreciable size. With but few exceptions these benign tumors were not the major indication for the removal of the uterus. It is impossible to estimate in how many of these women the neoplasms would eventually cause symptoms necessitating their removal, but such a possibility must be kept in mind.

Cesarean hysterectomy in placenta previa and abruptio placentae is an effective way of controlling blood loss rapidly. When bleeding cannot be stopped by the usual procedures such as tamponade and suture, the removal of the uterus is indicated. Obviously, in women who have had families the conservation of the uterus becomes of secondary importance. Patients with abruptio placentae who have extensive extravasation of blood into the uterine wall and environmental tissues, and in whom the uterus fails to respond effec-

tively to oxytocic drugs, should have hysterectomies. Although we know more about the defect in the blood clotting mechanism that may develop in some of these women, the removal of the uterus still remains a major step in the control of hemorrhage.
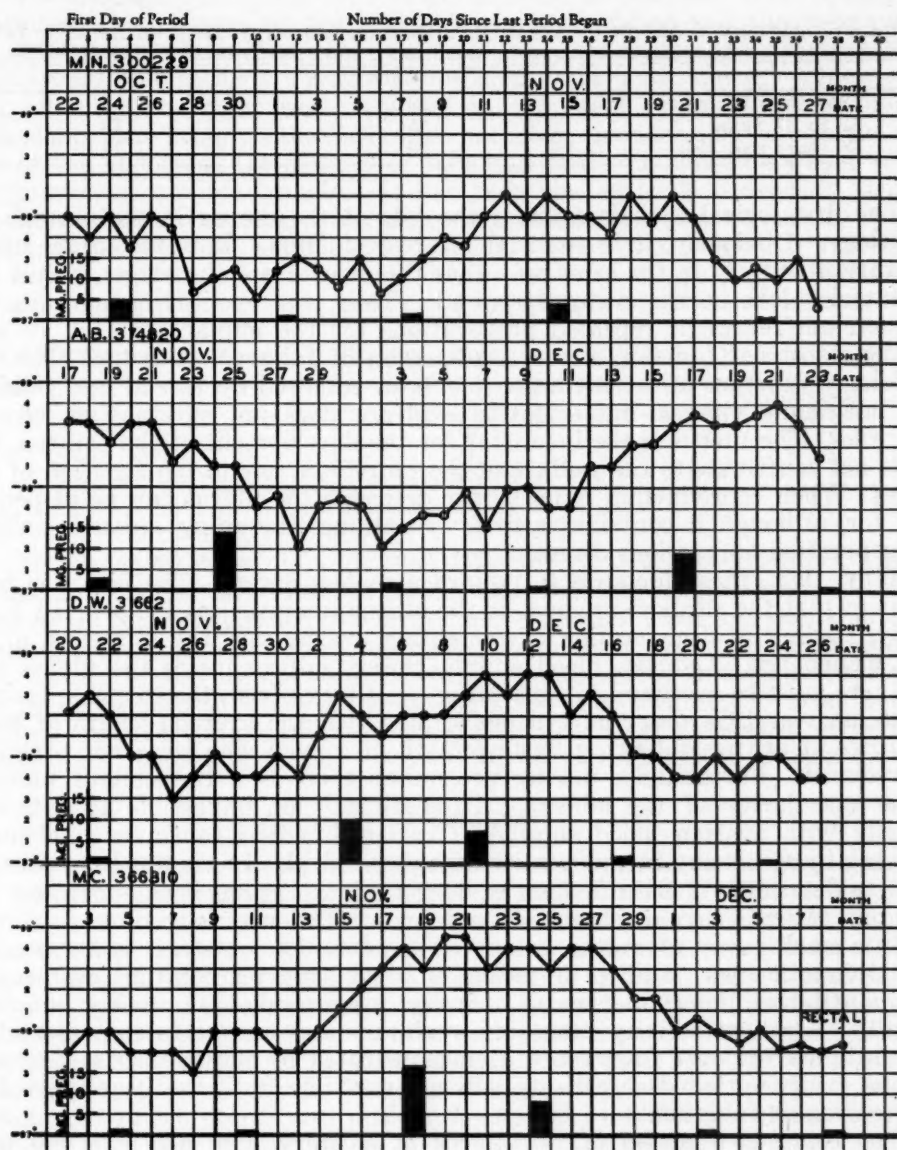

Fig. 1.—Basal body temperature graphs and urinary pregnanediol excretion in four women who have had cesarean hysterectomies. Cyclical ovarian activity has not been altered.

Cesarean hysterectomy was carried out for a variety of other indications for which abdominal delivery was the procedure of choice. In addition, future childbearing in many of these women was considered extremely hazardous, so that some procedure for the termination of the reproductive career was indicated. In a few individuals previous tubal ligation had failed to prevent pregnancy.

Operations other than cesarean section had been carried out on the uterus and adnexa in some patients. Others had a history of gross and disturbing

menstrual irregularities. The majority of the patients were in the middle thirties or older (Table IV). Thus, several factors usually entered into the decision to remove the uterus as the best expedient for delivery of the baby and the return of the patient to good health.

TABLE IV. MATERNAL AGE IN CESAREAN HYSTERECTOMY, JULY 1, 1947, TO APRIL 1, 1951

	COMPLETE	INCOMPLETE
Less than 30 years	19	8
31 to 37 years	55	18
38 years and older	26	14

The first logical consideration is the role of the uterus in the normal sex physiology. Obviously, it is essential for reproduction. It is the target organ for ovarian activity in the same way that the ovaries are the target glands for the anterior lobe of the pituitary gland. Thus, the cyclical changes in the endometrium represent repeated preparations for the implantation of an egg, and the menstrual function nature's admission of failure. It is true that this physiologic function of menstruation has been endowed by legend and folklore with imaginary virtues, but scientific evidence does not substantiate any of these roles. The uterus is the incubator for the development of the embryo, but it does not contribute to the welfare of the individual nor to the function of the ovaries. When reproduction is no longer desirable the uterus can be dispensed with, for, although it contributes little or nothing, the aging organ is subject to degeneration and serious disease.

Why, then, the reluctance to remove a useless organ? The idea has been prevalent that the surgical removal of the uterus compromises the ovarian blood supply, leading to degeneration of remaining ovaries and the induction of an early menopause. Ovarian blood supply closely approximates the uterus and great care must be exercised in separating the adnexa from the corpus. Indeed, Kretzschmar and Gardiner have demonstrated that the average length of functional life of ovaries following hysterectomy in women who were not pregnant was reduced. Fortunately, during pregnancy there is a tremendous increase in the vascularity of the adnexa. It is difficult or impossible to interfere crucially with ovarian blood supply. Ovarian function continues unchanged following hysterectomy in the women we have studied. It has not been possible as yet to determine if the life span of ovarian function has been shortened, because our patients have not been followed for a sufficiently long time.

In a small group of women who have had complete cesarean hysterectomies ovarian function was studied by means of basal body temperature graphs and the quantitative determination of urinary pregnanediol at weekly intervals (Fig. 1). Cyclical activity including ovulation and corpus luteum formation has continued for over four years, as demonstrated by these criteria. There is no good evidence that such activity will not continue until the usual period of waning ovarian function.

The complete removal of the uterus at delivery does not interfere with normal sex life; it actually improves it. Complete cesarean hysterectomy properly carried out so that none of the vagina is sacrificed and the vault is adequately supported results in an exceedingly long, normal vagina. In many of our women the usual speculum does not expose the vault adequately. This unusual roominess is brought about by the growth changes induced by the stimulus of pregnancy, resulting in much more favorable conditions postoperatively. The roomy, plastic vagina, combined with the freedom from fear of conception results in ideal marital life. Each patient in our series of complete cesarean hysterectomies was questioned at her periodic examinations concerning her marital life following surgery; they were in universal agreement on this

point. Thus, neither libido nor normal sex life is interfered with by the procedure.

The Treatment of the Adnexa

The management of the adnexa at the time of cesarean hysterectomy will depend on their normalcy, the patient's age, her wishes, and the judgment of the obstetrician. It will be noted that one tube and ovary were removed in the majority of the patients (Table V). Usually the most normal adnexa were left, although the right were removed in the event both sides were normal. This choice was made on the basis that pathology is more common on the right side of the abdomen; the absence of tube and ovary on this side would remove one source of possible trouble. It has been the author's conviction that the functional life of one ovary, carefully separated from the uterus to conserve ovarian blood supply, would be as long as that of two ovaries. Furthermore, the removal of the adnexa on one side reduces by one-half the likelihood of cystic changes in the ovaries, and, more important, hopeless ovarian cancer.

TABLE V. REMOVAL OF ADNEXA IN CESAREAN HYSTERECTOMY, JULY 1, 1947, TO APRIL 1, 1951

	COMPLETE	INCOMPLETE
None	10	22
Right adnexa	47	10
Left adnexa	28	7
Bilateral	15	1

In women 40 years old and older, bilateral removal of the adnexa was suggested and carried out 15 times in the 100 complete hysterectomies. Ovarian salvage in the twilight of the reproductive period is of questionable value. Waning ovarian function for a few more years does not compensate for even the little hazard of leaving the adnexa behind. Furthermore, menopausal symptoms can be suppressed so much better in the absence of declining ovarian activity. There is no harm in maintaining these women on a small amount of estrogen for a long time, thereby retaining for them all the advantages of ovarian function.

Technique

The technique of complete cesarean hysterectomy is no different from that of complete hysterectomy in the nonpregnant individual. The anatomic relationships of the uterus and bladder are easily discernible although there may be some ureteral dilatation (Fig. 2). The greatly increased vascularity of all the tissues, especially the enormously dilated veins in the broad ligaments, need not give trouble if all structures are doubly clamped, cut, and ligated.

It has been our practice to begin the operation according to our technique for laparotrachelotomy or the lower segment cesarean. The bladder peritoneum is incised transversely from one round ligament to the other, just below its attachment to the uterus and pushed downward by blunt dissection. The lower segment is incised longitudinally and temporary hemostasis obtained by broad Allis clamps on the cut edges. The patient is administered 0.2 mg. of ergonovine intravenously just as the baby is to be delivered, in order to facilitate the separation of the placenta.

After the placenta is out of the uterus the corpus and lower segment are packed with gauze. The incision is closed quickly by a running stitch. These procedures can be accomplished in several minutes; they will reduce the blood loss materially and provide a dry field for the removal of the uterus.

If the adnexa are to be spared, clamps should be placed as close to the uterus as possible. The individual bites should be small so that three separate bites usually are necessary to sever the adnexa from the uterus. Each pedicle

is ligated separately. The uterine vessels can be visualized. They are clamped close to the uterine wall so that the pedicle includes some of the uterine tissue. This same procedure is repeated on the opposite side (Fig. 3).

The bladder is now pushed carefully off the remainder of the cervix by blunt and sharp dissection. It is important not to dissect too far laterally, for this invites bleeding. The cervix is separated from its attachments by three small bites, each placed adjacent and lateral to it. In cutting the cervix away from the clamp, good pedicles should be provided. The first clamp catches the pericervical tissue, the second the cardinal ligament, and the third the uterosacral ligament and edge of the vagina (Fig. 4).

Fig. 2.—The posterior view of the uterus immediately following the delivery of the baby and placenta. Anatomic relationships of the various structures of importance in complete cesarean hysterectomy are illustrated.

The vagina is opened through a longitudinal incision in the lowermost portion of the cervix anteriorly. By the aid of forceps the cut edges of the cervix are pulled out of the vagina (Fig. 5). A gauze pack is pushed into the vaginal lumen carefully, to absorb the blood which invariably escapes into the vagina during the delivery and placental stage. This provides a dry field and reduces the hazard of peritoneal contamination. The vagina is now cut away from the cervix circumferentially. The incision is made in such a way that all cervix is removed, but little, if any, of the vagina. As the vaginal incision is continued the edges are caught by long forceps anteriorly, posteriorly, and laterally to expedite closure. The vaginal vault is closed and supported at the same time by interrupted sutures. The uterosacral ligament, the cardinal, the pericervical
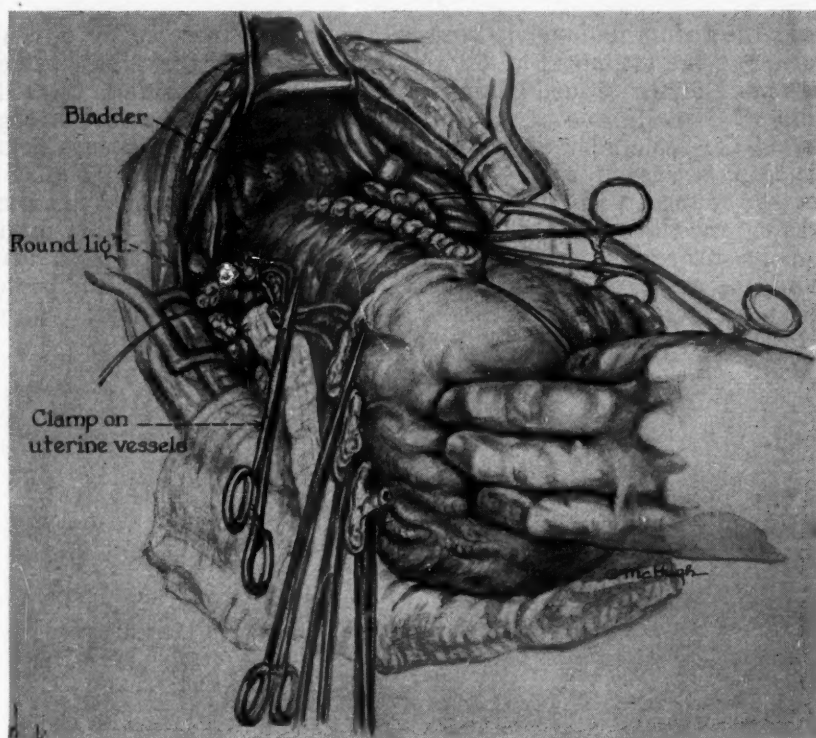
Fig. 3.—The adnexa are separated from the uterus in three small bites, the clamps being placed as close to the uterine wall as possible. Each pedicle is ligated securely before the next clamp is placed. The uterine vessels are now visualized and clamped, cut, and ligated.
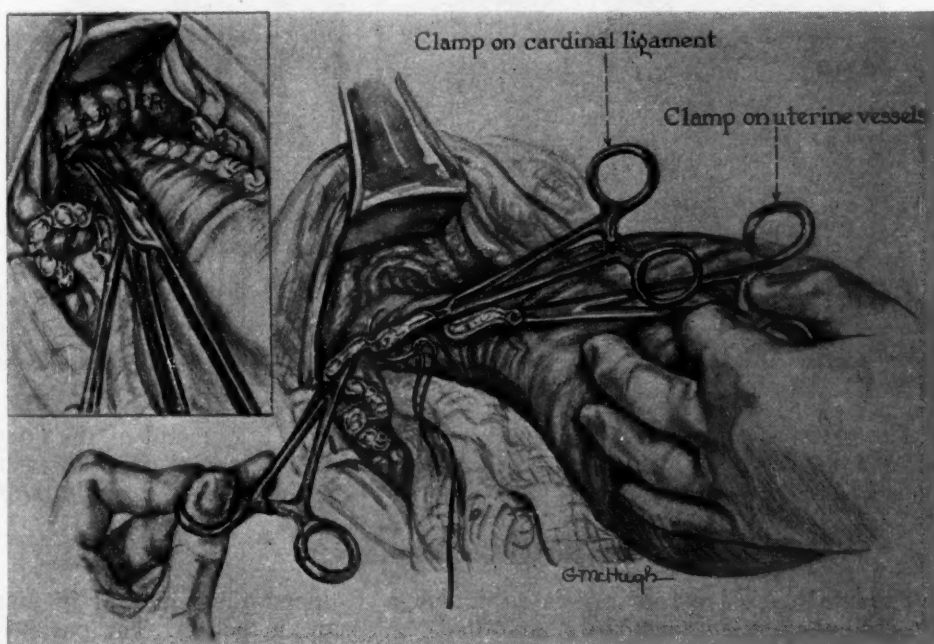

Fig. 4.—The bladder is now pushed off the cervix completely by sharp and blunt dissection. Care should be taken not to dissect too far laterally for this invites bleeding. The cervix is severed from its attachments by three small bites close to the cervix, the first embracing the pericervical tissue, the second the cardinal ligament, and the third the uterosacral ligament and edge of the vagina.

tissue, and the infundibulopelvic stumps are caught successively and attached to the corner of the vagina (Fig. 6). A second stitch fortifies these attachments and closes more of the opened vagina (Fig. 7). The other side is treated in the same manner. Usually one or two more interrupted stitches are necessary to approximate the remainder of the cut vaginal walls and to secure hemostasis. Peritonization is accomplished best when begun posteriorly (Fig. 8). The posterior leaf of the broad ligament and the uterosacral ligament are picked up first, and the procedure is continued in the customary manner, using interrupted or continuous sutures. Careful peritonization is desirable and, when completed, there should be no oozing areas. During the entire procedure the ureters and their peristaltic action are visualized easily, thereby safeguarding against any damage to them.
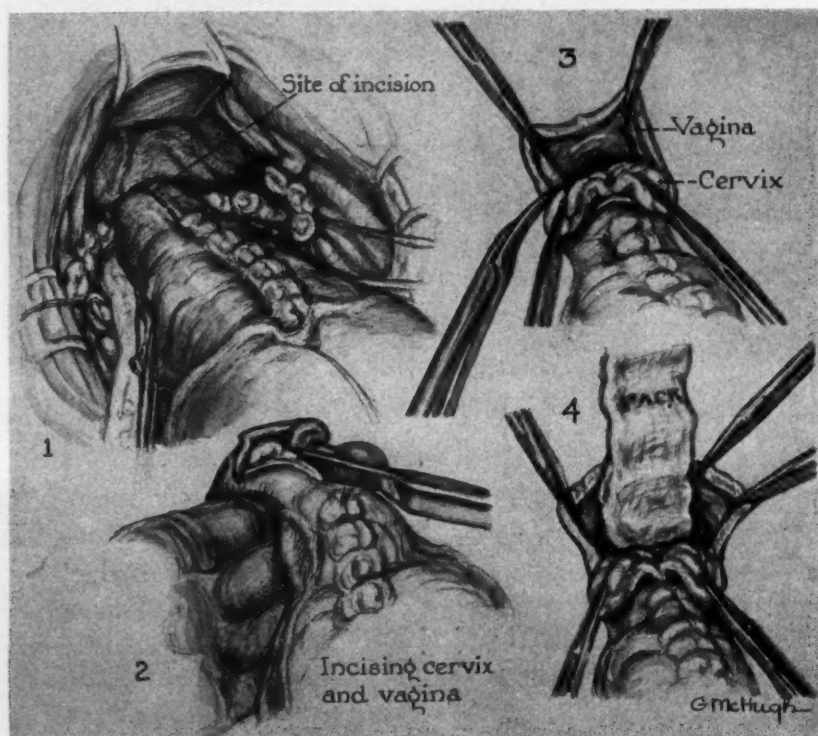

Fig. 5.—In View 1 the entire cervix has been freed from its attachments and the pedicles ligated. The dotted line indicates the site of incision through the anterior of the cervix. View 2 illustrates the incision through the cervix into the vagina. In View 3 the corners of the incised cervix are pulled upward by forceps and the vagina partially cut away from the cervix. In View 4 the pack is pushed into the vagina following which the incision separating cervix from vagina is continued posteriorly.

The gauze is removed from the vagina from below at the end of the operation. A Foley catheter, which has been placed into the bladder prior to operation, is allowed to remain for 24 to 36 hours when the patient is ambulatory.

Postoperative Complications

The postoperative recovery is rapid, usually uncomplicated, and in many instances even more uneventful than in simple cesarean section. The patient is allowed out of bed for a few minutes on the day after the operation and for increasing intervals on each succeeding day. The usual fluids are administered the first 24 hours and, if tolerated, fluids are given by mouth the second day.
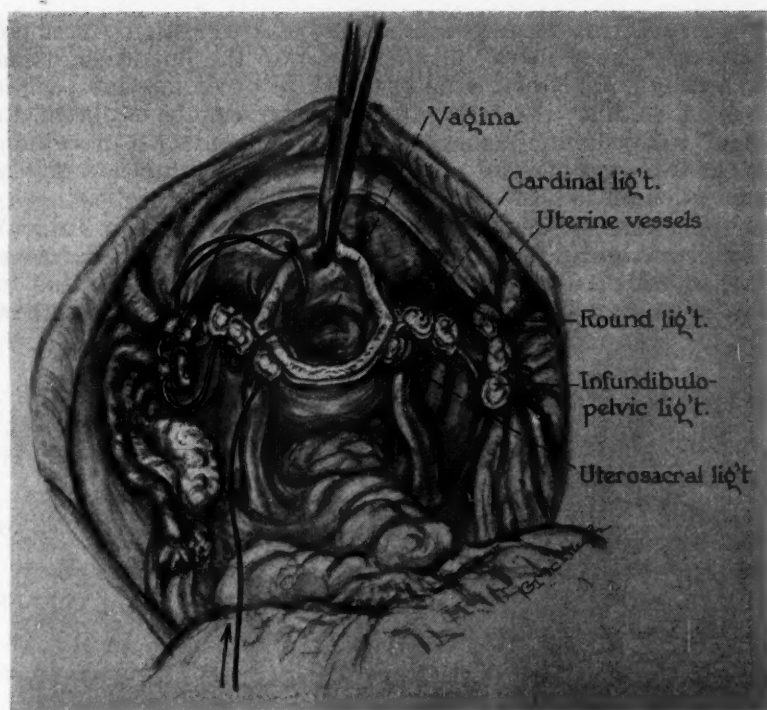
Fig. 6.—Closure and support of the vaginal vault are accomplished simultaneously by an interrupted suture through the corner of the vaginal wall, the uterosacral and cardinal ligaments, pericervical tissue, and infundibulopelvic stumps, successively.
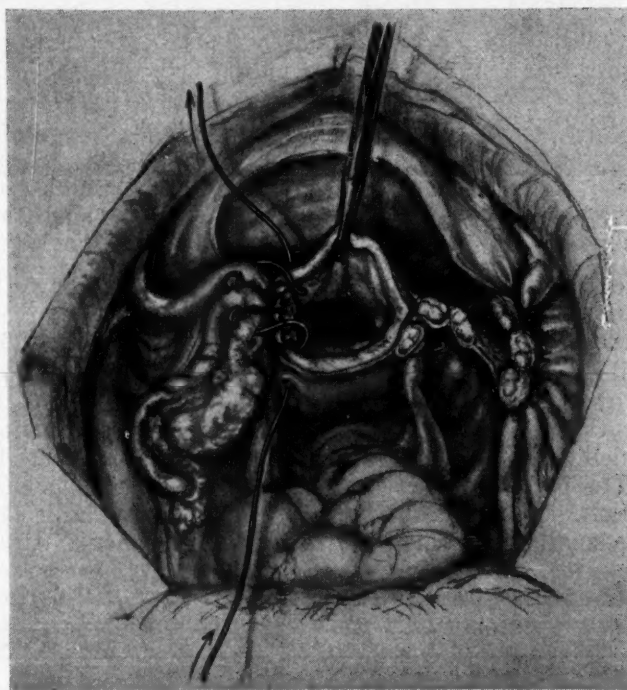

Fig. 7.—A second suture secures the pedicles to the vaginal vault and closes more of the opened vagina.

The diet is increased as rapidly as the patient's condition warrants. An indwelling catheter, placed in the bladder prior to the operation, remains until the patient is fully ambulatory, usually the third or fourth day. If the patient has difficulty in voiding, the indwelling catheter can be replaced for several days. Most of our patients have received 400,000 units of procaine penicillin twice daily for five days and sulfathiazole 0.5 Gm. four times a day until complete bladder function has been restored.

The complications in this group of patients are listed in Table VI. They were relatively few and did not result in residual sequelae. Gross hematuria occurred in two patients who had complete and in one who had an incomplete cesarean hysterectomy. This was apparently the result of bladder trauma. It cleared up after several days.
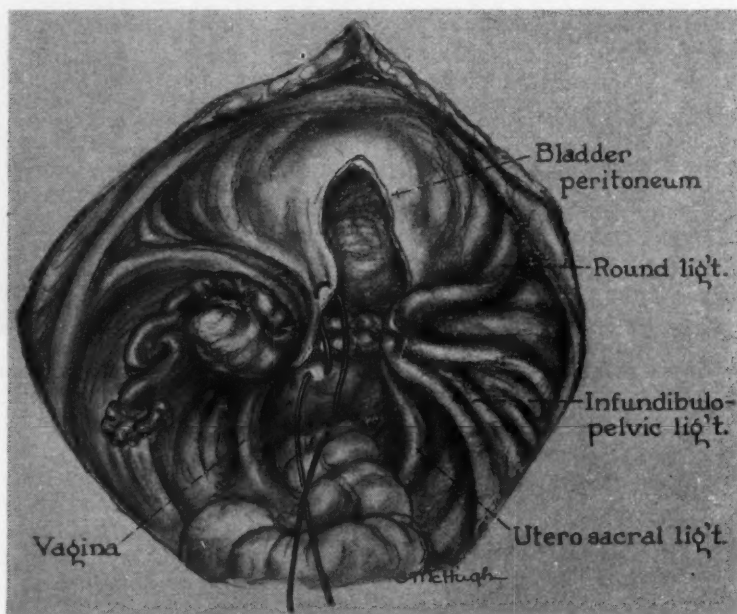

Fig. 8.—Great care should be exercised in peritonization, particularly on the posterior aspects of the adnexa and uterosacral ligaments.

The morbidity of complete cesarean hysterectomy compares favorably with that of the incomplete operation and with low or cervical cesarean section. The febrile index provides a graphic comparison of the two groups (Fig. 9).

One patient in each group developed abdominal distention, nausea and vomiting, and fever. In both instances the usual peritonitis regime was instituted promptly with rapid disappearance of peritoneal irritation.

Thrombophlebitis and phlebothrombosis remain a challenge to obstetricians and surgeons. The potential threat of serious embolic phenomena always exists in cesarean section. In our data the incidence of thrombosis is very low, but this group is too small from which to draw any conclusions. Prophylactic anti-

TABLE VI.   COMPLICATIONS, CESAREAN HYSTERECTOMY, JULY 1, 1947, TO APRIL 1, 1951

	COMPLETE	INCOMPLETE
Phlebothrombosis	1	2
Peritoneal irritation	1	1
Wound infection	0	1
Hematuria	2	1

coagulants should be explored more extensively in obstetric surgery, for thrombosis represents the most important hazard in our field.

Anesthesia

Anesthesia in abdominal delivery has always been a hazard which has been reduced greatly by developments in this field. Until the last five or six years most cesarean sections at the Chicago Lying-in Hospital have been done under local infiltration anesthesia with the use of procaine. This method is uniformly safe for mother and child, but it is time consuming, variable in success, depending on the skill of the surgeon, and it is not applicable to the nervous patient. Inhalation anesthetics increase the likelihood of pulmonary complications, lead to increased blood loss, and result in fetal anoxia (Table VII).
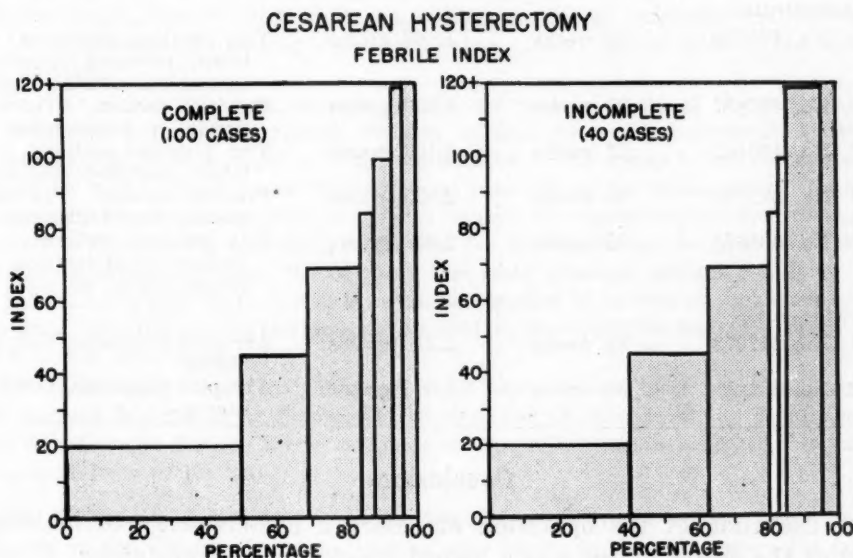

Fig. 9.—Comparative febrile index in complete and incomplete cesarean hysterectomies.

Spinal anesthesia carefully conducted by experienced personnel· is ideal for cesarean section. It is not without danger and occasionally a patient loses her life because of faulty technique, drug susceptibility, or overdosage. We have found that procaine in spinal fluid administered by the continuous spinal technique provides the greatest safeguards to the patient and her baby. This method allows the introduction of small amounts of procaine, 25 mg. or less at one time, and the level of anesthesia need be maintained no higher than necessary. The usual low or cervical cesarean section requires a total of 75 to 100 mg. of procaine, and the level of anesthesia is rarely above the costal margin. Cesarean hysterectomy may require as much as 150 or 200 mg. over a period of about one and one-half hours. It allows for perfect relaxation, so that the pelvic organs are approached with the greatest ease. This form of anesthesia contributes tremendously to this operation.

TABLE VII. ANESTHESIA, CESAREAN HYSTERECTOMY, JULY 1, 1947, TO APRIL 1, 1951

	COMPLETE	INCOMPLETE
Continuous spinal	87	22
Spinal	7	13
Local infiltration	2	5
Inhalation*	6	7

*Primary or supplementary anesthesia.

Perinatal Mortality

A list of stillbirths and neonatal deaths appears in Table VIII. There were seven deaths in 140 cesarean hysterectomies. The two stillbirths were the result of abruptio placentae. Of the five neonatal deaths, two infants weighed less than 1,500 grams and one died of erythroblastosis. It is doubtful that the method of delivery contributed to any of the fetal deaths. Nevertheless, the incidence of respiratory failure associated with resorption atelectasis and hyaline membrane is much higher in premature babies delivered by cesarean section and must always be kept in mind when abdominal delivery is considered.

TABLE VIII. PERINATAL MORTALITY, CESAREAN HYSTERECTOMY, JULY 1, 1947, TO APRIL 1, 1951

Neonatal Deaths.—			
1. No. 170950	26 weeks	1,060 grams	Two previous cesareans. In labor, ruptured membranes, incomplete uterine rupture
2. No. 486837	31 weeks	1,490 grams	Previous section. Placenta previa, in active labor
3. No. 450442	33 weeks	2,190 grams	Two previous sections. In labor, ruptured membranes
4. No. 321738	34 weeks	2,535 grams	Previous section. Placenta previa, erythroblastosis
5. No. 301624	35 weeks	2,608 grams	Two previous sections. Failure tubal ligation. Hypertension, fibroids
Stillbirths.—			
1. No. 517072	32 weeks	2,370 grams	Abruptio placentae, Couvelaire uterus
2. No. 461410	30 weeks	1,640 grams	Abruptio placentae, Couvelaire uterus

Conclusions

The extension of the operation of cesarean hysterectomy to include the removal of the entire uterus was a logical development in obstetrics; it follows the trend established in gynecologic surgery. Our increased familiarity with this procedure and our mastery of the few technical details inherent in surgery at the end of pregnancy have increased our enthusiasm for this operation to such an extent that it has almost replaced the incomplete procedure in our clinic. This brief and preliminary report records our experiences with complete cesarean hysterectomy in the hope that it may serve to stimulate others to do the operation when it is indicated. We realize that many data will have to be accumulated before this procedure can become standard practice in our large teaching clinics.

Discussion

DR. KARL WILSON, Rochester, N. Y.—Dr. Davis presents the perennial problem of total versus subtotal hysterectomy from a somewhat different angle. In my opinion, the same arguments for and against total hysterectomy hold true in connection with cesarean hysterectomy as are advanced in regard to hysterectomy in the nonpregnant individual. In advocating total removal of the uterus when a cesarean hysterectomy is done, I believe Dr. Davis is on solid ground, though advocacy of this procedure is somewhat belated in obstetric surgery.

The chief objection to the subtotal operation, as I see it, is the possibility of carcinoma developing in the remaining cervical stump. I have had that happen in one of my patients and ever since this tragic occurrence have been a strong believer in the total operation.

The total cesarean section hysterectomy is not as easy a procedure as the subtotal operation, and operative difficulties may ensue in particular on account of the marked displacement of the bladder and ureters in the later part of pregnancy, and on account of the greatly increased vascularity. Dr. Davis apparently had no difficulties along these lines in his series, but still accidents can happen as the result of these anatomical circumstances. I fear the results if the occasional operator resorts to the total operation.

Coming to indications, I find myself in some disagreement with Dr. Davis. In my clinic, there have been 651 cesarean sections of various types performed in some 30,000 deliveries, an incidence of 2.25 per cent. In 44 of these the uterus was removed at the same time, or 6.6 per cent of the cesarean sections, the majority being subtotal operations, and no maternal mortality occurred in connection with these hysterectomies. Our indications were four in number, and only four: (a) the presence of myomas of such number or size as to necessitate removal of the uterus; (b) uncontrollable hemorrhage after cesarean section; (c) in the past a few (9) uteri were removed on account of infection, and (d) in a few cases (5) as a means of effecting sterilization when consent for resection of the tubes could not be obtained.

Dr. Davis' indications go considerably beyond these. In 24 of his patients, namely, those presenting hypertensive disease, diabetes, cardiac disease, and leucemia, I assume the hysterectomy was done in order to effect sterilization. This seems to me to be an extreme procedure to carry out on women whose general condition is not satisfactory. I would also take issue with his idea of removing the uterus because the woman has attained the age of 40. To carry this hypothesis to its logical conclusion, one would advocate the removal of the uterus in all women beyond this age. As of today, too many cesarean sections are done. Though much safer than in past years, it still is not to be regarded as an entirely innocuous procedure. If too many unindicated hysterectomies are added to the operative total, the operative mortality is bound to be increased.

In conclusion, I believe that, in cesarean hysterectomy, the total operation is preferable to the subtotal, but the indications should be restricted to those involving definite pathology of the uterus except for the infrequent case where sterilization is indicated, but cannot be accomplished in a simple way.

DR. EDWARD SCHUMANN, Philadelphia, Pa.—It would appear from Dr. Davis' charts that in the Chicago Lying-in Hospital one woman in five who enters the institution for delivery by the comparatively simple procedure of cesarean section leaves without her uterus and also that about one woman in twenty who goes for the same purpose leaves her right ovary in addition. This seems to be a distinct violation of our modern concept of the reproductive organs which is tending far more toward conservation than destruction.

Dr. Davis gives a list of indications for this complete hysterectomy after cesarean, very few of which seem valid to me, since I feel very strongly that the only reasons for hysterectomy at this time are uncontrollable hemorrhage, rupture of the uterus, or multiple fibroid tumors, such cases occurring in a small number of our cesareans.

Dr. Davis also states rather definitely that the removal of the entire uterus in a young woman does not contribute to any difficulty in her sex life or the psychology of the patient, and here also I differ very greatly. The suppression of menstruation in any young woman with the complete psychic revolution which accompanies it is a very serious difficulty. Furthermore, the fact that these women are inevitably rendered incapable of further childbirth is a serious matter, indeed. As to the utilization of hysterectomy in sterilization, the whole procedure seems to me like cracking nuts with a sledge hammer. A simple Pomeroy ligation will accomplish the same purpose with infinitely less trauma. I confess that possibly age has increased my feelings toward this whole problem and has rendered me completely unsympathetic with any rate of 20 per cent hysterectomy in cesarean section.

DR. THADDEUS MONTGOMERY, Philadelphia, Pa.—In considering Dr. Davis' presentation one must agree with the fact that, as the frequency of cesarean section is increasing and its indications are being broadened, we are also progressively decreasing maternal and fetal mortality. A certain portion of this decrease may legitimately be attributed to the

use of cesarean section in situations where formerly a more traumatic form of vaginal delivery might have been employed. Technical improvements in operative procedure and anesthesia, and the application of antibiotics have made it possible to do this operation with a minimum of risk. As a result, there is a temptation to do at the one sitting a little more than simple hysterotomy, such as myomectomy, oophorectomy, appendectomy, and, in the cases cited by the author, a high percentage of sterilizations and complete hysterectomies.

My own definition of "conservative" obstetrics is the thoughtful selection and careful application of procedures which will conserve maternal and fetal life. If more cesarean sections are necessary in order to accomplish this purpose, then I would still call it a "conservative" procedure.

However, when it comes to the question of sterilizing each patient at the time of a second cesarean section, or of employing abdominal hysterectomy as a method of sterilization, of performing a complete hysterectomy instead of a ligation of the tubes or simple hysterectomy, and of removing one ovary at the time of hysterectomy in order to prevent the possibility of ovarian carcinoma developing in that ovary, we are getting a little bit beyond the conservative application of cesarean section.

In the first place, I am amazed and concerned about the freedom with which some obstetricians and gynecologists recommend and perform sterilization, apparently simply because the abdomen is opened for some other gynecologic procedure, or because the patient has requested it, or because the patient has simply had two births by cesarean section. Apparently, the assumption on the part of the physician is that the patient and her husband know what they want and are entitled to have this procedure done.

There are several reasons to look upon this situation seriously. In the first place, a sterilization or a hysterectomy is an irrevocable and irreversible annulment of the patient's childbearing function, which is not sanctioned on minimal indications by the laws of most of the States in this country. Second, it is a procedure which does not take into account the subtle psychological effect which the operation may have upon relations of husband and wife, and certainly does not take into account the fact that loss of a child or children, remarriage of one or the other partner, and a change in point of view of the two marital partners may make them most desirous in the future of having further children. I doubt very much that a young woman in her twenties or early thirties is in any better position to select sterilization intelligently than she is to consider discontinuation of an unwanted pregnancy intelligently.

As to performance of sterilization at the conclusion of the second cesarean section, I think that this is in the majority of cases utterly unnecessary. While the attending obstetrician should have the permission of husband and wife for sterilization, he should decide upon the operation at the time and on the basis of the condition of the uterus when the cesarean section is done. If the uterine wall is in good condition there is no reason for either ligation or hysterectomy. In support of both of these theses I may say that every year I see a number of patients who have had sterilization done at the second cesarean section or done in the course of some other pelvic operation, who deplore and regret the fact that they submitted themselves to such a procedure.

It is the duty of the attending obstetrician to take a long view of these subjects, to talk them over thoroughly with the patient and point out the reasons why such a procedure should not be done, and if there is no medical indication for the sterilization, to refuse firmly to do it. There are other methods of temporarily avoiding pregnancy which are satisfactory enough to control childbearing without resorting to a complete ablation.

As to the use of complete hysterectomy instead of supracervical hysterectomy when sterilization is performed, the subject seems of no paramount consequence. If the patient has had all of her children by cesarean section, it is not likely that the cervix has suffered much trauma and there is probably less likelihood of her developing cancer than would occur otherwise. Again, the tendency of many operators is to leave the cervix in when performing hysterectomy on a very young woman if the cervix appears normal, etc. Complete hysterectomy at full term with the patient not in labor is technically somewhat more difficult than a simple cesarean section with ligation of the tubes and I am not sure that the present low morbidity

and low mortality of the operation would be conserved if all operators started doing complete hysterectomy under these circumstances. At the moment, it would seem to be one of the lesser obstetrical problems that we have to face.

As to the removal of one ovary at the time of a complete cesarean section in order to lessen the likelihood of ovarian cancer occurring in the future, one would have to consider the logic of removing various organs to prevent remote possibilities of cancer occurrence. Personally, it would seem much more logical for the operator to remove the left breast during the course of his cesarean section. A simple mastectomy could be done very easily in twenty or thirty minutes and cancer is more likely to occur in the breast than in the entire genital tract put together. I doubt, however, that such a recommendation would prove very popular.

DR. DAVIS (Closing).—I wish to thank Dr. Karl Wilson and the other Fellows who were kind enough to discuss my paper. I expected a difference of opinion for any change in our traditional thinking is worthy of serious discussion. The pattern of obstetric care has undergone great changes in recent years. The spectacular reduction in the hazards of childbearing has given us an opportunity to evaluate our methods in the light of the mother's health and welfare. We must no longer be satisfied with bringing a baby safely into the world but we should do everything possible to assure the mother happy and healthy years in which to raise that baby.

We have demonstrated that the complete removal of the uterus can be done safely at cesarean section by well-qualified specialists. The end results of such a procedure are excellent physiologically and psychologically. Why then the violent reaction to our suggestion that an abnormal uterus be removed at the end of the reproductive career? The uterus that is altered by fibroid tumors, scars from previous sections, or a diseased cervix is a liability to the patient. It contributes nothing to her well-being. We have not advocated more cesarean sections and, actually, our data indicated that we did no more abdominal deliveries at the Chicago Lying-in Hospital in 1950 than in 1930. However, we feel that the removal of an abnormal uterus at cesarean section is constructive surgery for it may spare the patient premenopausal difficulties, later pelvic surgery, and even cancer of the uterus. I am sure that future experience will justify the preliminary observations we have presented today.

RADICAL HYSTERECTOMY WITH BILATERAL PELVIC LYMPH NODE DISSECTIONS. A REPORT OF 100 PATIENTS OPERATED ON FIVE OR MORE YEARS AGO*†

Joe Vincent Meigs, M.D., Boston, Mass.

(From the Vincent Memorial Hospital, the Pondville Hospital, and the Palmer Memorial Hospital)

FOR some years prior to 1939, after an experience of over 25 years with the radiation treatment of cervical cancer, dissatisfaction was felt with that treatment for this disease as given in our clinics. Visits were made to the operative clinics in Europe and America. Dr. Victor Bonney of London was the first operator visited and although he was fast losing his material to the radiologists he still felt the importance of a surgical approach to the disease. Such interested surgeons as Philipp and Wanekros were visited in Germany, and, as more surgery was watched, enthusiasm for the surgical approach began. The late Dr. Fred J. Taussig demonstrated to this writer the importance of the careful removal of the pelvic nodes during his operative procedure. Dr. Taussig's method of dissecting the nodes and their channels en bloc suggested to me the idea of combining his pelvic node dissection with the radical removal of the uterus and its "parametrium." The late Dr. Frank Lynch of San Francisco confirmed the author in his idea that radical surgery could and should be attempted in the face of widespread acceptance of radiation as the proper attack on epithelial neoplasms of the cervix. In 1939 a few patients who had had full radiation and who had persistent disease were operated upon. The results were not spectacular but, with the advent of sulfonamides to avert infection, it was decided that a definite program should be outlined with the expectation that the operation, using all the methods of modern surgery, might cure as many patients as radiation therapy. There are those who will say that our radiation was not heavy enough and not given properly, and that, if it were, all cases would respond satisfactorily. To our satisfaction this has not proved to be true and we in our clinic recognize that there is a difference between patients who respond to radiation and those who do not. This is not the place to argue this point but our Vincent Memorial Laboratory is now geared to the study of the problem and many of the early findings support the idea of resistance and sensitivity.

Material

In 1939 an operative series of 100 patients was begun with the author as the surgeon in all of the patients. No staff member or resident was allowed to interrupt the sequence until 100 patients had been operated upon. The series

developed slowly and in 1946 the 100th patient was operated upon and the series completed. Five years have now passed, the follow-up has been thorough, and the results are presented to you in Tables I and II. These results are not the true results in this series as 15 cases have been excluded by the pathologists in their final estimation of the pathological findings. This report follows and includes the cases previously published, and, although the pathologic findings were satisfactory to me and to our pathologists at that time, they do not now satisfy our final estimation of the stage of the cancer. In other words, Tables I and II represent the very best results we could obtain, especially Table II, which excludes patients who died of intercurrent disease and who might be excluded because of autopsy and other findings. These extraordinary results are not our present estimate of the results of the surgery of this disease and our new results are presented toward the end of the paper.

TABLE I. RESULTS FIVE YEARS FOLLOWING OPERATION

Total No. Cases	100	Living 78 or 78.0%
Stage I	72	Living 61 or 84.7%
Stage II	28	Living 17 or 60.7%

TABLE II

Died of intercurrent disease—5	
Hypertensive heart disease	
Cancer of stomach	
Cancer of lung	
Meningitis	
Diabetes	
Excluding the above:	
Living five years	82.1%
Stage I	89.7%
Stage II	63.0%

It was essential that the surgical mortality match the mortality figures in the cases treated by radiation. With careful surgery and the use of sulfonamides and antibiotics 100 patients were operated upon with no hospital mortality. The operation is now a successful surgical procedure and does not carry the great danger that it did in former days. Over 280 combined radical hysterectomies and pelvic lymphadenectomies have been done by all members of our staff, including our residents, with but two deaths, one due to embolism, and one to rupture of an aneurysm of the circle of Willis. The operation has become a part of our regular attack upon cervical cancer and at the present time at least 50 per cent of all our patients are operated upon. We are so satisfied with the results and so sure that we know what we can accomplish that we have decided that a more intelligent radiologic attack must be made upon the disease to determine whether or not we can produce results with radiation comparable to our surgical results.

A paper written in 1950 by Dr. John McL. Morris and the author demonstrated to us that our radiation treatment and its results were unsatisfactory, yet our figures, recorded according to the International Classification, compared favorably with the figures in other clinics of this country when their figures were changed from other classifications to the International Classification. It is obvious to us that our radiation results are not good enough and certainly not so good as the surgical results. Stimulated by the reports of the Radiumhemmet, the Royal Cancer Hospital in London, and the Manchester group we are at present joining with our radiologists in an attempt to set up

similar methods of dosage and treatment and we hope to be able to approach
their figures and thereby show that radiation should continue as a treatment
of choice. The nearly exact measurement of dosage in gamma roentgens has
made our more or less haphazard measurement in millicurie hours or milligram
hours seem obsolete and unsatisfactory. Consequently Dr. Morris is in Europe
to study how we may best change our radiation attack and prove to ourselves
that it is a comparable method of treatment. Having a good surgical base line
and a good milligram and millicurie radiation base line we hope with new plans
to surpass anything we have yet done.

Certain of our changes in treatment are in line with Dr. McKelvey's sug-
gestions, such as nutritional and preparational care of the patient before, dur-
ing, and after radiation treatment. His results are so superior to any other
radiation results that is is essential that we adopt his methods when they differ
from ours. It is quite possible that his types of patients, nationalities, etc., may
be so different from ours that we cannot approach his excellent results. Never-
theless, we are endeavoring to adopt all the important and different aspects of
care and treatment of those who better us and, in addition, by doing careful
research on these patients, demonstrate what we should do to assure better re-
sults. In our clinics in Boston we believe in radiation sensitivity and resistance.
We are sure that the radiologist begins his treatment, in Stages I and II, with
positive nodes present in at least 20 per cent of his cases and we are thus
skeptical of too good results in these stages. Both radiological and surgical
treatment must be available and after research into sensitivity and resistance
we feel that radiation will be the treatment for certain patients and sur-
gery for others. The attack on cancer is not surgical alone nor radiologic
alone but patients should be selected for one or the other. We definitely do
not believe that the combination of radiation and surgery in the same patient is
satisfactory or safe—one or the other should be used by a process of intelligent
selection, and *not* both.

Radical Abdominal Hysterectomy with Bilateral Pelvic Lymph Node Dissection

Our operation is not the Wertheim operation, and if Wertheim's report
of 500 patients operated upon and published in the *American Journal of Ob-
stetrics* in 1912 is read, it should be obvious that it is not the same. Wertheim
did *not* routinely dissect the pelvic lymph nodes. He did it only after palpa-
tion and inspection and occasionally only upon opening the retroperitoneal
space and viewing the area. From a large experience we believe that positive
lymph nodes cannot be determined by inspection, palpation, or visualization
and that the only proof that lymph nodes are positive or negative is examina-
tion in the Pathology Laboratory after their removal. Thus it is not correct
to call the operation that we have been doing a Wertheim operation. Dr. Taus-
sig carried out careful, nearly en bloc, dissections of nodes of the pelvis and
his attack, added to the Wertheim radical hysterectomy, is the operative pro-
cedure we are discussing. Dr. Taussig showed nodes to me no larger than the
head of a match that contained cancer, and other larger and softer ones that
had no cancer in them; these facts we have proved many times in our work. It
is probably true that if the nodes were cut by serial section a greater percentage
would be found to contain cancer. The young pathologist in training usually
selects the nodes to be examined microscopically, thus it must follow that some
are missed. One section of each node is not sufficient. I have been criticized
for not calling this operation a renaissance of the Wertheim operation, but it
is *not*. It should be called by the long name given as that is the only ade-
quate, descriptive name for our operation.

Wertheim's Problems and Ours

It is interesting to read Wertheim's article for it is like reading one of our own. He ran into the same problems that we do. Ureterovaginal fistula puzzled and troubled him and his number of fistulas is about what ours will be when we have accomplished 500 operations. The reason for the development of a fistula is not clear. No doubt lack of blood supply, trauma, and leaving ureters in a pool of infected blood have to do with their destruction. One great comfort to us is the fact that nearly all cure themselves spontaneously if left alone long enough, i.e., the fistula heals, but usually with the loss of function of the kidney that is involved. It has been extremely rare for us to be forced to remove a kidney once the injured ureter has ceased to drain.

Occasionally removal of positive nodes is very difficult and sometimes the dissection has to be omitted and the operation abandoned; Wertheim recognized this fact. He was against radical surgery in those patients whose aortic nodes were involved. Wertheim had sepsis to contend with, i.e., peritonitis, but in this age we have very little of that. He found it necessary to devise a clamp that would go across the vagina below the growth so that spillage would not occur. This is omitted in our cases so that a much larger vaginal cuff is obtained. Strangely enough even without radiation in the cervix before operation and without cauterization of the growth before operation, recurrence in the vagina has been very rare. Perhaps implantation of tumor into raw surfaces is not so easy as it would seem to be. Vesicovaginal fistulas troubled Wertheim somewhat but this has rarely been one of our problems. This is a complication that we have avoided; how, I do not know. Suffice it to say that in only two instances out of over 280 operations has this complication been met with.

The Reasons for Surgery in Cancer of the Cervix

I have explained the reasons for our doing surgery many, many times and I have continued to believe in those reasons: recurrences after radiation, the problem of radiation resistance and sensitivity, lack of bowel injury, and lack of node sterilization by radiation. I see no indication to add to the reasons or to subtract from them. The operative procedure and the surgical convalescence are much less strenuous for the patient than x-ray treatment and radium. I have had the opportunity to speak with many who have had both and in nearly all instances the patient states that surgery is less difficult. Our surgical operation becomes more and more radical as we become more and more adept, and more and more complications occur for there are more possibilities for injury of nerve and blood vessels, etc. Suffice it to say that we feel that surgical treatment is satisfactory. It is superior to full radiation treatment, and it is as safe. The above are our reasons for urging it upon patients and very rarely have we regretted our choice.

The Material and Selection of Patients for Operation

The material for our series has been from private cases, from the wards of the Vincent Memorial Hospital (a Gynecologic Service affiliated with the Massachusetts General Hospital), from the Palmer Memorial Hospital, and from the Pondville Hospital (Massachusetts Department of Public Health). At first the patients were very carefully selected and but few were operated upon and those only excellent risks, but after the operation was established and its possibilities explored the only guide is the patient's physical condition, *not* the size of her tumor. We have found that we can operate upon patients in Stages I, II, III, and IV but for this operation we have selected those in Stages I and II

in most instances; a few Stage III cases have been included. Our decision for operation does *not* depend upon the extent of the tumor in the cervix, vagina, and paracervical and paravaginal tissues but only upon whether or not the patient is a good risk and whether or not we feel we can safely operate upon her. This after all is the essence of good surgery. I have been accused of operating upon only the "chronic appendices" of cervical disease. That accusation is not true for we operate upon all patients from whom we feel it is possible to remove their cancer if they are in physical condition to stand it. We must not forget that we have radiation, which is generally considered the *best* way to treat the disease. If a patient's condition does not seem to be such that we feel we can successfully operate upon her it is much better to give radiation therapy.

Cancer in Situ and Cancer in Situ with Minimal Invasion

In this report patients with cancer in situ, intraepithelial, or incipient cancer have been excluded. Some of our cases previously included in the invasive stage have recently been excluded by our pathologists after re-reviewing the material. Their knowledge of in situ cancer has developed more and more.

Stimulated by the ideas and suggestions of our pathologist, Dr. Benjamin Castleman, we have subjected all of our cases to a re-review. Strangely enough not all have agreed in the reports and diagnoses as made in this series. After viewing all the slides and conferring with the pathologist I had felt that not one of these cases could be called what is understood as "cancer in situ" for we had previously excluded all cancers in situ, and there were a number of those where we had done the radical operation. Now it is necessary to come before you and to report that 13 of our 100 cases are now classified as cancer in situ or cancer in situ with minimal invasion, and two are now considered to be cancers of the endometrium with involvement of the cervix. One cancer of the endometrium with direct invasion of the cervix and one with the tumor extending through the cervix to present a large mass at the external os have been excluded. In this report the above 15 cases will be discarded, leaving 85 cases that are admitted to be invasive cancer of the cervix. All of the above 15 patients survived five years. Our pathologists think that all such cases should be cured by surgery as they feel that these cases do not represent true cancer of the cervix. Thus it is not possible for me to report 100 patients with true, invasive cancer followed for five years but we can report the results of 85 cases of unquestionable cancer of the cervix five years after operation. This is a much more satisfactory group to report and there can be no question, at the present writing, that our 85 cases are true cervical cancers. Taking out these patients naturally decreases the percentage of good results in Stage I; the group in Stage II remains the same and the incidence of lymph node involvement is increased.*

In re-reviewing the slides of these patients we did not leave the diagnosis to any single pathologist for many saw the slides; if any in the group of the pathologists raised the question or said they thought the slide was representative of cancer in situ it was excluded. It is important in such a report as this to give only the results of operation in real cervical cancer. The decision as to whether a tumor is in situ, is in situ with minimal invasion, or represents early invasive cancer is a difficult one, and this whole question should be discussed at greater length by a group of pathologists who are qualified to lay down rules that will be accepted by all. Without doubt, for I have seen the slides in all cases reported here and have been over them with pathologists, we are discarding cases

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*One Boston pathologist believes that six of the excluded cases are true invasive cancers, and another believes that two of the excluded cases are invasive. This is obviously a very confusing problem for pathologists.

of early, invasive cancer, but until a definite group of criteria are laid down it is far better to exclude any possibly questionable cases than to include them. It is my feeling that in cancer in situ the entire depth of the surface epithelium must be involved in definite cancer without any break-through of the basal epithelium or break-through of the basal epithelium of a gland that may be involved.

Glandular invasion is not invasive cancer. If there should be a very slight or microscopic break-through of either of these two areas, a diagnosis of cancer should be made, but if the break is only microscopic and the tumor not visible to the naked eye it should be excluded. The diagnosis of true cervical cancer should be made only when the tumor is visible or can be curetted from the endocervix and when it has broken through the basal layers of cervical and glandular epithelium. True cervical cancer must be seen macroscopically as well as microscopically. These are criteria we have laid down for ourselves and we feel that everyone who has previously reported patients cured by radiation in Stage I should review their slides with the idea of reporting only true cervical cancer. That these rules will be questioned and not agreed upon is understood, but if this paper stimulates thought and interest in the disease it will have done great service to its proper treatment. All of our patients with cancer in situ who have been excluded have lived for five years. Although this does not rule out the fact that these patients may have had cancer of the cervix, yet the fact that all are cured shows that such cancer as they had was definitely curable.

This problem has been discussed a great many times by all of us concerned in the study of cervical cancer and we are not in total agreement. I cannot but believe that this report of 85 cases is much more valuable to those of us interested in this disease than it would have been if we had included the too early cases and thus increased our survival rate. The results are so satisfactory that we will probably choose to continue this method of treatment until something better comes along. As the responsible surgeon in all of these cases and responsible for papers written in the past I must ask you not to be too critical of our past reports; those papers were written with the idea that only invasive cancers were in the group. However, more modern and more enlightened understanding has changed certain of our ideas. We hope that you will receive this report with the understanding that although all our 85 cases are considered as invasive cancers as of today, no one knows what they may be considered in the future.

The Operation

The operation has been described many times and is illustrated in Meigs and Sturgis' *Progress in Gynecology,* Vol. II. There have been only a few changes but those that have occurred have been significant. Dr. C. Kaufmann of Marburg, recently a visitor in our clinic, described the tissue removed from around the uterus, cervix, and vagina as "Franz Joseph's whiskers," meaning that we should remove as much paracervical and paravaginal tissue as the former Emperor of Austria had whiskers, and he stated that the more "whiskers," the better the operation. This graphic description stimulated us to do more radical surgery and we have already found his suggestion of value. The tissue about the bladder, the vagina, and the cervix is of great importance and it is found in two fossae: one in relation to the bladder, the so-called subvesical fossa, and one in relation to the rectum, the so-called subrectal fossa. The two fossae are divided by what we elect to call the "web." This web is composed of Mackenrodt's ligament, and the vessels going to and from the vagina and cervix from the internal iliac artery and vein. The web reaches to the floor of

the pelvis. It is a very definite structure, and troublesome vessels lie in it, as do lymph nodes and channels. The "web" is removed by clamping and tying with stitch ligatures at the lateral pelvic wall. It can also be dissected carefully and its many veins and arteries tied off separately. The two fossae run to the lateral pelvic walls and to the floor of the pelvis and contain what we call the paracervical and paravaginal tissues. This structure has been confused with the parametrium which, according to Piersol's Anatomy, is that tissue within the two leaves of the broad ligament surrounding the uterus. It is perhaps best to say that one must remove the parametrium and, in addition, the pararectal, the paracervical, and paravaginal tissues. It is very important that this be removed because, since insisting that this be done and since the areas have been sectioned separately, we can easily see where we have missed lymph channels and lymph nodes containing cancer. There is one disagreeable result of the more radical surgery in that more bladder difficulties occur and a longer time is necessary for bladder function to return to normal.

Lymph Nodes

Positive lymph nodes have been frequent, the obturator and iliac group being involved most commonly. It is possible that lymph channel and node involvement will be present more often in the paracervical and paravaginal tissue than was formerly thought. In this series of patients 22.4 per cent had positive nodes; in Stage I, 17.5 per cent, and in Stage II, 32.1 per cent. The more widespread the disease the more involvement of lymph nodes. We have been able to remove the common iliac, external and internal iliac, ureteral, obturator, presacral nodes, and the nodes from the fossae. No attempt has been made to reach all the sacral nodes but some of them have been removed with our more extensive type of surgery. We have attempted to remove nodes from above the bifurcation of the aorta in but very few instances. If the chain of nodes running up the aorta is enlarged and considered to be positive no radical surgery is entertained. Of 19 patients with positive nodes 5, or 26.3 per cent, have lived five years. This is very satisfactory, and it is an improvement over radiation for it is our belief that the latter probably will not cure positive nodes. There is great dispute about this. Dr. Morton's figures have been quoted to prove that some patients with positive nodes are cured by radiation treatment. Our figures refute his and it is uncertain which is correct. However, I believe that it is the opinion of most that destruction of cancer in pelvic nodes has *not* been proved and, as Dr. Taussig said, there is no reason to believe—even if the tumor has been made to disappear from the nodes—that a recurrence will not take place in them. This discussion is still academic. The outlining of nodes by placing silver dura clips on the node-bearing areas, as suggested by Dr. Langdon Parsons, is very important, for it is obvious that x-ray treatment as given in most clinics does not reach the most distant nodal areas that are removable by surgery. This in itself makes it evident that x-ray treatment as given today cannot accomplish what surgery can.

Postoperative Complications

Our most frequent and difficult complication is ureteral fistula, which has been discussed above. Bladder problems are frequent. Apparently the operation, and especially the more radical surgery, injures the nerve supply to the bladder and prevents normal function. Patients are kept on constant drainage by means of a Foley catheter for seven to eight days after operation. Upon its removal it is rare for a patient to void spontaneously and empty the bladder. Usually the catheter will have to be replaced and, by trial, emptying will take

place. It often takes three weeks before voiding is easy and spontaneous, and in many instances the patient cannot tell when the bladder is full and has to be put on a definite four hourly voiding routine. This complication does not prevent their discharge from the hospital but it does mean that they are bladder conscious for a long period of time. Patients may not be able to recognize a full bladder for as long as a year or more after operation. Before leaving the hospital most of them have a residual urine of one to two ounces. They do well and only occasionally have cystitis or pyelitis. This is not a healthy condition but no real disasters have occurred because of it.

Fifty of our patients have had intravenous pyelograms done from three and one-half to ten years following their operations and, surprisingly enough, few had any permanent changes in the ureter or kidney pelvis. Eight, or 16 per cent, showed difficulty with the urinary tract. There were five with absence of dye on one side due to operative injury of the ureter and fistula, two blocked ureters due to cancer, and one patient was operated upon for stone in the kidney; 84 per cent of those who submitted to pyelograms showed normal upper urinary tracts. This study was carried on to prove that years afterward cicatrices following the surgery did not constrict the ureters and cause destructive processes in the ureters and kidneys. All patients void well within less than a year of their operations and although some do not have perfect bladder function none are invalids in any way because of urinary tract disability.

Bowel problems are no different from those occurring following any pelvic surgical procedure. Obstruction is very rare. Ileus occurs occasionally as in any group of surgical patients. No rectovaginal or other bowel fistulas or injuries have occurred following surgery.

Unfortunately sexual intercourse is interfered with in a definite percentage of cases, for the vagina is shortened. In only one instance was this serious enough to end in a separation of the couple. In most instances, in spite of a short vagina, sex relations have been satisfactory to both parties, though anatomically this does not seem possible.

Phlebitis and embolism are rare and only one patient died of this disaster in 280 cases; she had a sudden embolism without any previous evidence of phlebitis. This absence of embolism is fortunate for the veins of the pelvis are exposed and subjected to definite amounts of trauma during the operation. Our other death in the 280 cases was one due to a rupture of an aneurysm of the circle of Willis and might have occurred at any time.

Radiation and Surgery

In our clinics we are avoiding the combination of radiation therapy and surgery. No doubt the local lesion can be destroyed by radiation in a certain percentage of cases, but the firm, fixed pelvis so frequent following combined radiation and surgery does not follow surgery alone. Radiation causes fibrosis, arteriosclerosis, and interference with the blood supply to the pelvic organs. The blood supply to the bladder, ureters, and rectum is interfered with and poor blood supply to these may be the cause of very serious difficulties. However, it is interesting that in our series more fistulas occurred in patients who did not have preoperative radiation. In a larger group of patients we believe the reverse would be true. The fact that in our patients more positive nodes were found in patients who had had radiation does not prove that radiation may not injure the tumor in lymph nodes; it is possible that in such a small group of patients the true picture is not seen. Many believe, and we are among them, that radiation will *not* destroy cancer in nodes and that, even if it does, it is no guarantee that the tumor may not recur in the nodes or that if they are not

removed tumor may not later metastasize to them. The combination of radiation and surgery does leave a hard, frozen pelvis. It is easy to tell on examination when the combination has been used. This hard, firm type of pelvis may easily lead to later involvement of the ureter in scar tissue, and hydroureter and hydronephrosis may follow. The surgery itself is not necessarily more difficult following radiation; as a matter of fact, often it is easier, but from our knowledge of radiation reaction we feel that loss of blood supply and cicatrization may be of serious import. At the present time because of the very few recurrences in the vagina or in and about the scar in the vagina we feel that local destruction of the proliferative tumor by radiation before operation may not be necessary or wise. We have not used the cautery to accomplish the destruction of the local lesion, for recurrence is rare in the vagina. Sometimes radiation makes it extremely difficult to separate the cervix and vagina from the bladder and injury to the bladder in radiated tissue may lead to bladder fistulas. There is no proof that radiation is dangerous in patients subjected to surgery but it is our feeling at this writing that it is not to be preferred but to be avoided.

Results

There was no postoperative mortality in the first 85 patients. These were given proper sulfonamide and antibiotic treatment and no patient died because of her operation. It is impossible to deny the value of sulfonamides, antibiotics, blood transfusion, and proper conditioning of the patients. We feel confident of good postoperative results in patients with cancer of the cervix and do not anticipate that they will die following radical surgery.

Of the first 85 patients whom we have been able to follow for five years 74.1 per cent have survived (Table III). This we consider to be a very creditable showing. Again let me remind you that the patients were selected because of their physical condition for surgery and not because of the extent of their disease. There were early tumors in the series but many large, infiltrating tumors were operated upon. No matter what the size of the lesion the patients were not subjected to surgery if their physical condition showed them to be poor candidates for a serious operation. Dividing the cancers into stages, 80.7 per cent of the Stage I patients are alive and 60.7 per cent of the Stage II patients are alive. Patients with Grade I cancers did better than those with Grade II. The subsequent deaths and the presence of lymph node involvement followed closely the stage and grade of the lesion. In Stage I, of 57 patients, 17.5 per cent had positive nodes and of those with positive nodes four are living and well at five years. In Stage II, of 28 patients, 32.1 per cent had positive nodes and only one of them survived five years. Patients with positive nodes can be salvaged; it is interesting to note that, of 22.4 per cent of patients with positive nodes, 26.3 per cent, or five out of 19 cases, are living and well at five years. This does not mean that they are cured but at five years they are apparently well and without disease. In the entire group there were six, or 7.2 per cent of patients, with ureterovaginal fistulas. Surgeons will always have to face this problem. Undoubtedly as more ureteral blood vessels, both longitudinal and lateral, are protected and as less and less oozing occurs in the pelvis with subsequent infection fewer fistulas will result. We recognize and agree with the criticism of the operation because of ureterovaginal fistulas, but it must not be forgotten that a certain number of fistulas follow the best-given radium and x-ray therapy. These 85 patients may be a fortunate series and the results may not be repeated for we are now doing much more radical surgery. I know, and all who read this paper should realize, that the operation done upon these patients over five years ago is not the same as that which can be done in 1951.

In our cases radiation did not increase the salvage nor did it increase the numbers of fistulas, which is the reverse of what should be expected. We are satisfied that radiation should be limited to the group not selected for surgery. After noting the results of treatment in over 2,000 cervical cancers, we should aim our research at selection of cases for radiation and for surgery. Probably certain cases should have been radiated and certain others operated upon. This problem will be settled on a basis of radiation sensitivity and radiation resistance, and it is hoped that some time in the future we will be in a position to select. The fact that the results in these 85 patients are as good as in any group treated by radiation in Stages I and II encourages me to continue to use surgery as a method of treatment for some cervical cancers.

TABLE III. PATIENTS OPERATED UPON FIVE OR MORE YEARS AGO

Total	85	Living 63 or 74.1%
Stage I	57	Living 46 or 80.7%
Stage II	28	Living 17 or 60.7%

TABLE IV

GRADE	NO.	PER CENT	LIVING		POSITIVE NODES	
			NO.	PER CENT	NO.	PER CENT
I	7	8.2	6	85.7	—	—
II	31	36.5	21	67.8	7	22.6
III	36	42.3	26	72.2	10	27.8
IV	3	3.5	3	100.0	—	—
Adenocarcinoma	6	7.0	5	83.3	2	33.3
Adenoacanthoma	1	1.2	1	100.0	—	—
? grade	1	1.2	1	100	—	—
Total	85		63	74.1	19	22.4

TABLE V. POSITIVE NODES

Total number	19	22.4% of 85 cases	
Living	5	26.3%	
Stage I	10	52.6%	Living 40.0%
Stage II	9	47.4%	Living 11.1%
Grade II	7	36.8%	Living 14.3%
Grade III	10	52.6%	Living 30.0%
Adenocarcinoma	2	10.5%	Living 50.0%

TABLE VI

Preoperative radiation 38 (44.7%)
    Living 26 (68.4%)
    Positive nodes 9 (22.3%)
    Fistula 3 (7.8%)
No preoperative radiation 47 (55.3%)
    Living 37 (78.7%)
    Positive nodes 10 (21.3%)
    Fistula 5 (10.6%)

On our wards where careful studies are being carried out more patients will receive radiation from now on. We feel we know what results to expect of surgical treatment but we do not know the possibilities of more perfectly given radiation. We recognize the lack of success in radiated cases in ours and many other clinics but this will be corrected in our hospital to the best of our ability. It will be necessary to pattern our treatment on that used in Sweden, Paris, Manchester, and London, and to watch McKelvey's work in Minnesota.

I feel that even then the radiation results will not be a great improvement over what we can accomplish by surgery and that surgery in the good-risk patient will be superior.

Comment

In this report the results in 85 patients subjected to surgical operation for cancer of the cervix are presented. Our operation at the beginning of this series was not so radical as it is now and this change has resulted in an increased incidence of bladder complications. We have had trouble with the ureter and we hope to lessen our incidence of this complication but doubt if it can be eradicated. Surgery has a definite place in the treatment of this disease, even if it does not appeal to all students of cervical cancer. We hesitate very seriously to recommend surgery but we believe it is fair to support those interested in surgery and especially those in a position to do radical surgery. However, too few have attempted to learn the surgical approach from those who have studied it. The author felt it was necessary to visit Europe, St. Louis, and San Francisco before he could commence his series. Many surgeons are attempting to do radical surgery without any preliminary observation or real thought concerning the operative procedure. Reports from other clinics purporting to do the radical operation suggest some are *not* doing the operation and do little more than a total hysterectomy. Their end results will certainly condemn the operation. It is fortunate that our first 85 patients have proved so satisfactory. Our results will be improved upon and the mortality equaled. Those who fall far below this standard will probably be among those who do not know how to choose cases or how to operate upon them properly if they do choose surgery. It is not fair to criticize a procedure if the procedure is not carried out properly. In our clinic we recognize our weakness in the radiation field and are now doing our best to correct our methods. We will visit and seek knowledge wherever it is to be found and eventually we will be in a position where we will know equally how to apply radium and x-ray treatment and to do radical surgery. Anything short of a complete armamentarium must be followed by inferior results. Lack of knowledge and ability should not condemn a good procedure but shows ignorance on the part of those directing the attack on the disease.

The combination of radium and surgery may eventually be proved to be valuable but at the present time we feel that each should be used alone in order to avoid the higher incidence of complications that seem to attend their combined use. Our greatest contribution is the fact that this operation can be done safely and with considerable success, and as far as we are concerned it represents an advance in the treatment of cervical cancer. We are not trying to compete with radiologists but are trying hard to improve their ability to give radiation by recognizing the extent of the disease and the areas that should be treated in the pelvis. Radiation is not simple and we believe requires the assistance of a physicist and certainly requires first-hand knowledge of the Swedish, French, and English methods. Some time laboratory studies upon patients will point out those who should be operated upon, those who should be treated by radiation, and those for whom it is useless to do anything. Cancer is cancer but in my opinion there are many different types and kinds of cancers and further investigation by special staining, by tissue culture, and by transplantation into animals and the recognition of changes in normal and tumor tissue following radiation will lead us to a more intelligent application of our knowledge of how to destroy or prevent growth.

Conclusions

1. This series of 100 patients with cancer of the cervix has been reduced to 85 because we feel, and especially and rightly our pathologist, Dr. Benjamin

Castleman, feels, that 13 cases should be called cancer in situ and 2 others, cancer of the endometrium.

2. The reasons for the change in pathologic diagnosis are that our concepts have altered materially in the last few years. In certain cases, however, all slides were not available for re-examination, some were labelled "mostly in situ," others were called epidermoid carcinoma, and the diagnoses of a few graded (Grade I, II, or III) cancers were considered incorrect. In many instances I felt confident of the presence of invasive cancer but have been overruled and probably correctly.

3. It is then obvious that this series represents true cervical cancer and the results are satisfactory.

4. The operations have been done in selected patients, i.e., selected for the surgical risk, *not* the extent of the disease.

5. Lymph node involvement is quite high, in 22.4 per cent, and yet 26.3 per cent of these have survived for five years.

6. Radiation has had but little effect upon the cases in this series as to length of life, node involvement, and fistula formation.

7. The surgical procedure is a satisfactory one and is probably a real aid in the treatment of this disease.

8. Radiation treatment in this country is not so well given as it should be and it is essential that greater study be given to this form of therapy.

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Discussion

DR. HERBERT SCHMITZ, Chicago, Ill.—The industry and earnestness of the author in his attempt to solve the riddle of how to treat cervical carcinoma have won him the admiration of his colleagues in this country and abroad. I would say that Dr. Meigs, since his first publication relative to his plan to re-evaluate the surgical attack for this type of cancer, has been the most extensively quoted worker in the field. In haste, let me add that his presentations have too frequently been misquoted. The present contribution, dealing with the five-year salvage in 85 patients known to have invasive carcinoma, will be no exception.

The inclusion in Table I of those cases deleted by the pathologists as being preinvasive carcinoma in 13 instances and endometrial carcinoma in 2 others may again cause confusion as there may be those who will accept the five-year results in the 100 cases feeling that they were in the original operative series, and, therefore, should be included to demonstrate the safety of the operative procedure. The low risk attendant on this operation, when performed by a capable surgeon familiar with the minutest details necessary to execute the procedure properly, has already been demonstrated in previous reports by the author. This

re-evaluation, however, should not be interpreted as reason for accepting surgical treatment
in favor of radiological, for Dr. Meigs clearly states that "both radiological and surgical
treatment must be available and after research into sensitivity and resistance we feel that
radiation will be the treatment for certain patients and surgery for others." When one form
of treatment is instituted through choice and not because of definite evidence in favor of its
employment, disaster is inevitable.

The question of which tumor is radioresistant and which is radiosensitive is a problem
being studied by many investigators who agree for the most part that microscopic character-
istics of individual cells or groups of cells in biopsy specimens taken before therapy are in-
adequate. The only accurate method at present is a test of sensitivity similar to a test of
labor. If cells recovered by smear methods and repeat biopsy fail to show response known
to result from certain amounts of radium and x-ray, then surgical procedures should be
instituted as soon as the erythema has subsided and before fibrosis has begun. In our ex-
perience such a procedure does not present unsurmountable technical difficulties.

That "true cervical cancer must be seen macroscopically as well as microscopically" is
debatable. I believe most students of this disease accept evidence of tumor emboli in vessels
or lymphatics as evidence of true invasive cancer, even though the disease may be preclinical
macroscopically.

The constant repetition by Dr. Meigs of his opinion that lymph nodes invaded by car-
cinoma are resistant to irradiation is not substantiated by the studies of Morton, Taussig,
or Henriksen. May I add to this evidence of sensitivity the observation in many reports
that, as irradiation techniques with higher voltage x-ray improved and heavier dosages were
distributed throughout the pelvis, survival of patients in Stages II and III i. reased. The
radium dose aimed at the disease in the cervix having remained the same, undoubtedly the
factor responsible for this observation is the destruction of disease in the pelvic lymph nodes.
Of the patients with positive nodes who survived in this report, four were in Stage I where
the disease was still confined to the cervix and nodal involvement probably confined to the
area within Zone A of the Manchester plan of radiation therapy. In this area a dose, lethal
to most cancers, may be delivered. Only one patient with positive nodes in Stage II survived,
demonstrating that surgery as well as radiation is inadequate when the disease is too wide-
spread. In Dr. Meigs' series showing nodes following radiation, it is my opinion that radium
alone was employed by him preoperatively and the dose, therefore, inadequate to deliver a
lethal tumor dose beyond the confines of the cervix. It would be enlightening to know in
which of these cases active tumor was still evident in the cervix. The work of Otto Saphir
of the Michael Reese Hospital confirms Dr. Meigs' suspicion that serial section of nodes
would reveal many more to be invaded by disease, for he, in serial sectioning of all nodes
removed at the time of radical mastectomy, showed that many nodes thought to be free of
disease on single section examination were actually positive.

When the selection of patients for irradiation therapy is carried out as carefully as
the selection of patients for surgery, and when the details are as carefully observed during
the preparation for and care during the course of irradiation, then the end results from
this therapy will be more pleasing to our essayist and his co-workers. McKelvey, in obtain-
ing his splendid results, supported and nursed his patients as carefully as those he subjected
in his clinic to radical hysterectomy and pelvic lymph node dissection. Trauma, infection,
underdosage, overdosage, delays, and systemic disease such as circulatory or excretory im-
pairment, anemias, diabetes, malnutrition, etc., influence the course of the patient receiving
irradiation as much as they do the course of the patient subjected to surgery. When Dr.
Meigs relegates those cases not fulfilling his demands for a suitable surgical risk to radia-
tion therapy, he is making comparison in his clinic impossible. For these patients will not
respond as well to radiation and cannot, therefore, be compared with the selected surgical
group. No matter how carefully we select our patients so as to obtain maximum results
with either form of treatment, we are still confronted with the pertinent questions: what
are we to do with the remaining cases, and what are our over-all results with the patients
who sought admission to our clinics?

Dr. Meigs is careful to recount his extensive travels to study the surgical techniques in a number of clinics before instituting his own study, and he tells us that as he has developed his skill the operation has become more extensive and may well lead to increased salvage. The postoperative complications described as occurring in the urinary tract are more frequent than the damage reported sustained due to irradiation used to treat this stage of the disease, and the annoyance to the patients must equal the discomfort of radiation cystitis or fibrosis. Careful shielding of the bowel should prevent major damage to that structure, and stricture due to fibrosis resulting from irradiation effect is rarely encountered in our series.

We are, therefore, of the opinion that the reasons as here stated for employing surgery in selected cases are not valid and the only conclusion permissible from this excellent presentation is that certain cell types of cervix cancer are radioresistant and are, therfore, best treated by surgical means. The procedure for selecting these cases is still lacking.

Dr. Meigs is to be congratulated on his splendid results which are a direct reflection of his surgical skill.

DR. RICHARD TE LINDE, Baltimore, Md.—I want to add my word of thanks for this very courageous experiment which Dr. Meigs has been carrying on these past several years. It has taken a tremendous amount of hard work and now for the first time he can give us a sizable series of five-year results. It is extremely difficult to compare his results with the results of irradiation because there is not an exactly comparable series treated with irradiation. I think Dr. Meigs did right in excluding cases of carcinoma in situ, even when questionable. If all carcinoma in situ is now tossed into Stage I it is going to throw our statistics off when we get to comparing results of present-day therapy with that of earlier years. For example, McKelvey has reported excellent results so I asked him if he included carcinoma in situ and he said he did. We know we can cure almost 100 per cent of the cases in the in situ stage with surgery and a very high percentage by irradiation. If they are included in Stage I, the statistics are not comparable to previously recorded statistics. I have just looked at our figures for the 1944 patients and we had 70 per cent five-year salvage with irradiation for Stage I; that is, irradiation plus a few selected cases which were operated upon. It is our plan in our clinic to do the typical Wertheim operation on those Stage I cases not responding to irradiation. In those cases we attempt to do the operation Dr. Meigs has just talked about and I believe the operation has a definite place there. I doubt whether the differential between the operative and irradiation salvage will prove to be sufficient to cause us to abandon irradiation in favor of surgery in the usual case of Stages I and II. One reason for this is the fairly high percentage of urinary fistulas that result from surgery. It is about equal to the percentage resulting from irradiation. But there is an important difference. The surgical fistulas occur in the Stage I and II cases in which there is an excellent chance of cure of the cancer but the irradiation fistulas occur in the cases of Stages III and IV. These latter women have a poor chance of longevity anyway and therefore a fistula in them is usually a relatively minor tragedy.

DR. HOWARD C. TAYLOR, Jr., New York, N. Y.—Dr. Te Linde has stated there is no series in existence which in a controlled fashion compares the two methods of treatment—irradiation and radical hysterectomy. That is almost correct except for a small series of cases representing one year's work in the files of the Memorial Hospital in which alternate cases were treated, one by radiation and one by radical surgery. These cases were treated in 1945. A preliminary review of these cases was made by Twombley about one year ago, giving four-year results. There were about 90 cases in all, approximately 45 treated by radiation and 45 by radical surgery.

These cases were limited to Stages I and II and all were certified by the clinician as being operable cases in the technical and medical sense. The secretary of the department indicated on the basis of her records whether they were to be operated upon or radiated. It is my opinion that only an experiment of such a type, eliminating a selection so far as

is possible, will give us information as to the merits of the two methods of treatment. The required five-year period was not complete when the first review was made but after four years the results appear to be almost the same for the two series of cases.

I would submit that we make very little progress toward a final decision between radiation and surgery when we compare the results of one clinic with those of another. I hope that this type of clinical experiment, which I think is justified because there is at present little to choose between the two methods, could be reproduced elsewhere. We have been discouraged about continuing this at the Sloane Hospital because we have a relatively small number of cases and an accumulation of a sufficient material would take a long time. Perhaps if several clinics combined their results, each following such a system of alternation, we could get an answer. We will certainly not find out whether surgery or the radiation method is better by our present statistical approach unless some unexpected new principle enters into the therapeutic possibilities to upset what is now a very close balance.

MR. CHARLES READ, London, England (by invitation).—I would also like to pay my tribute to Dr. Meigs' surgical skill and the results he showed. It is interesting to me to see that he found positive glands in 20 per cent of Stage I cases, which is what we have found in our series. I wonder if Dr. Meigs selected the Stages I and II cases which were ideal surgical risks?

So far as radium and surgery are concerned, I agree that the primary treatment is by radium and that one must select cases for surgery. I have been interested in the number of cases thought to fall into Stages I and II which were found at operation to be more advanced. This presents difficulty at operation because it means that more extensive dissections than originally planned have to be embarked upon, and on several occasions I have had to resort to an anterior exenteration on the spot. Looking at our previous Wertheim specimens after operation, I have been impressed with the inadequacy of clearance of the growth, and I am sure we would see better results in some of these cases if we did an anterior exenteration operation instead of confining it to the Wertheim type of clearance.

DR. VIRGIL S. COUNSELLER, Rochester, Minn.—I do not believe I have ever heard a more honest or sincere discussion of surgical management in such a serious disease.

My predecessor, Dr. James C. Masson, found over the years that there were certain lesions which could be treated surgically rather than by radium. About 80 per cent of the carcinomas which we see in the clinic are Stage I and Stage II. The many recent discussions of intraepithelioma carcinoma are making people more aware of carcinoma of the cervix, so that they are coming to their physicians earlier. This provides an opportunity to treat patients who do have such lesions by means of radium or surgery, whichever seems indicated.

In our group of cases, from 1930 to 1950, Stage I and Stage II lesions are predominant, although there are some in Stage III and Stage IV. Studies of morbidity are interesting. Early, there was morbidity in 93.5 per cent of cases; then this percentage declined to 51.5 in recent years. This gradual reduction perhaps is due to the effect of antibiotic agents. Postoperative deaths decreased from 12.9 to 8 per cent. We now have a series of 130 without a death. The survival rates are interesting; in fact, they are similar to those shown by Dr. Meigs: 86.2 per cent of patients have lived more than five years; patients who had Stage I and Stage II lesions have a much higher survival rate. When dissection of nodes has shown them to be normal, survival rate is high.

DR. ALEXANDER BRUNSCHWIG, New York, N. Y. (by invitation).—I am very grateful for the opportunity to discuss Dr. Meigs' outstanding presentation before this Society. I for one think this is one of the most important contributions that has been made in recent years to the subject of treatment of carcinoma of the cervix. Dr. Meigs has said so much and has said it so well that there is not much to add.

The point that the Wertheim operation does not represent the maximum surgical effort possible cannot be emphasized too strongly. I wish the term ''Wertheim operation'' could be dropped from current parlance.

It is impossible for me to present five-year results because the surgical program at Memorial Hospital has not been in existence that long; it started in September, 1947. *We have not selected our patients.* We have operated on recurrent caricnoma, primary carcinoma, recurrences involving the bladder and involving the bladder and rectum. In all we have about 400 cases but of this group only about 240 have had hysterectomy and node excision. Among that group there have been two instances of surgical mortality, making an incidence of 0.8 per cent; in addition, three others succumbed to complications more than one month following operation but they were still in the hospital. One was an elderly woman who died of intestinal necrosis; another had had four operations and had been irradiated sufficiently to result in necrosis of the blood vessels and she died of massive hemorrhage. The third died of complications following an operation performed by the urologic service for repair of a fistula six weeks following operation for cervical cancer. Medical complications such as diabetes or cardiac conditions are not considered contraindications to operation; for instance, we had one woman who weighed 226 pounds with a recurrent carcinoma of the cervix and she was operated upon. Age and obesity did influence the kind of operation. We do not perform radical hysterectomy and node dissection in all cases. In very obese and elderly women we do radical vaginal hysterectomy (Shauta) if the uterus comes down easily. If this could not be accomplished, then we do a "Wertheim" type operation. A patient 63 years of age who received radical abdominal hysterectomy is living and well three years later. In another unselected case a woman who weighed 310 pounds was operated upon in October, 1947, for a small cervical carcinoma, and she is still living and well.

Dr. Meigs is very self-critical because he threw out cases that he says might have made his results appear more striking than they do. This might well be emulated in the future by others reporting on cancer therapy. We should all have a rigid review of microscopic sections so as not to include carcinoma in situ. The latter lesion is not carcinoma and I believe that many of the very high incidences of cure reported by irradiation include cases of carcinoma in situ.

Another interesting point is a salvage of 25 per cent of patients with lymph node metastases. That is a straw in the wind because the series is not big but, if it is further substantiated, it will have to give rise to serious reconsideration of the training programs for gynecologic surgeons for the future to provide for more surgical work than is usually the situation at present. I venture to predict that surgery will assume a more important role in the treatment of carcinoma of the cervix, not only in primary carcinoma but in the attempt to cope with recurrent carcinoma in the region of the cervix and recurrence involving the bladder and rectum. Skill acquired as the result of training and experience cannot be passed on to an individual and I agree with the discussants that we must continue to teach and state officially that radiation is the treatment of choice in carcinoma of the cervix in general hands. The established role of radiation in the treatment of cervical cancer is widely acknowledged but conditions change in medicine as in everything else, and a newer surgery has come into being. The experiences with the "Wertheim operation" are obsolete and these should not be referred to or help up in comparison to modern radiation therapy. I think Dr. Meigs deserves great credit for being one of the first in this country to realize that a new type of surgery has come into being and he has applied this brilliantly in the treatment of cancer of the cervix. And again for emphasis, his rigid self-criticism in the reporting of his cases should serve as a criterion for emulation by all of those who will report results of therapy in carcinoma of the cervix, regardless of what methods or combination of methods are in question.

DR. LEWIS C. SCHEFFEY, Philadelphia, Pa.—There is one phase of the discussion of Dr. Meigs's outstanding presentation, to which I add my word of admiration, that has not been touched upon. That is our great responsibility as teachers when dealing with the surgical phase of the treatment of cervical carcinoma. Many students today, at least in our experience, ask why we do not operate on all of our cases and say that general surgery teaches local excision as a primary principle in the treatment of cancer. The student, and

the intern, and the resident in graduate training as well, too often do not discriminate between the sharp criteria that Dr. Meigs has laid down as the basis for a successful surgical approach to cervical cancer therapy, and the uncritical attitude of those who urge ''hysterectomy'' in principle without qualification as to why, when, and how.

The point I wish to make is that we as teachers should impress our students, undergraduate and graduate alike, with the fact that 75 per cent of the patients we see from day to day are not in Stages I and II, and that irradiation is still the treatment of choice in the vast majority of patients with cervical carcinoma; furthermore that brilliant results have been obtained with irradiation in the receptive host. Hysterectomy for cancer of the cervix is not all that the term implies because we are seeing more and more patients coming to our clinic with relatively early recurrence after surgical procedures of an ill-chosen or inadequate nature, and with recourse then to nothing other than irradiation.

Let us familiarize our students and those in graduate training with the problem in its entirety, stressing the major role that irradiation plays and also the great need for individualization rather than generalization, hoping at last to reach that Utopian era when all patients come to us with early lesions, or better still with the diagnosis of ''carcinoma in situ.'' What I have said is in no way critical to Dr. Meigs' brilliant achievement, based as it is on the sound experimental performance of a master surgeon.

DR. MEIGS (Closing).—Something should be said concerning the selection of patients, as I have been accused of operating upon only the ''chronic appendices'' of carcinoma. We insist that the patient be in good physical condition and that her serum and blood chemistries be satisfactory. The extent of the growth does not matter so much. We do not yet know how to take care of the ureters but we are learning more and more. The treatment of positive lymph nodes is really important and the effect of both surgery and radiation upon them deserves more investigation.

EFFECT OF RADIATION ON METASTATIC PELVIC LYMPH NODE INVOLVEMENT IN CARCINOMA OF THE CERVIX*

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CARCINOMA of the cervix is perhaps the most important lesion encountered by gynecologists. In Arkansas, during 1948, there were 236 deaths from cancer of the uterus, which is nearly 2.5 times the 99 maternal deaths. The figures available from other parts of the country suggest similar ratios, with cancer of the uterus being responsible for from 2 to 6 times the number of maternal deaths. These figures represent the great strides made in maternity care and, while much is yet to be accomplished, most maternal deaths are now avoidable if both the patient and physician follow the well-established principles (Table I).

This is not the case with carcinoma of the cervix. There are no symptoms of early cervical cancer. Not only do most patients present themselves to the physician with relatively well-established tumors, but our methods of treatment are far from satisfactory. Thus, the best figures available show a mortality rate of from 60 per cent to 70 per cent within five years.

Clinical experience has established that deaths from carcinoma of the cervix are usually due to involvement of the structures in the broad ligament. Patients do not die of cancer of the cervix but of cancer of the parametrium.

This is not a new concept and history reveals many efforts to handle this problem. The struggles of J. Marion Sims to eradicate the local lesion were as ineffective as his efforts to persuade the "lady managers" to permit him to continue his care and studies of these unfortunate women in the Woman's Hospital.

TABLE I. DEATHS FROM CHILDBIRTH AND CANCER OF UTERUS, 1948*

	CHILDBIRTH	CANCER OF UTERUS	RATIO
Arkansas	99	236	2.3x
Alabama	188	406	2.0x
Iowa	47	263	5.0x
Kentucky	115	372	3.0x
Michigan	117	681	6.0x
New York	256	1,678	6.5x
Oklahoma	56	245	4.3x
Tennessee	142	387	2.3x
Virginia	113	359	3.0x
National Figures	4,130	17,120	4.0x

*From the *Federal Security Agency Bulletin.*

The uterus is a nonvital organ and its removal is technically easy. Yet, despite the many varied efforts at surgical extirpation, the clinically unsuspected extensions of the carcinoma to the parametrium and pelvic lymph nodes destroy two-thirds of the women afflicted with this disease.

Wertheim and others of the radical surgical school devised many operations to extirpate the extensions of the carcinoma to the pelvic lymph nodes. Despite their skills and the recent popular re-exploration of this procedure, the *over-all* survival of these patients continues to be low. The effectiveness of primary surgical attack on this disease appears to be limited to early and carefully selected cases.

With the advent of x-ray and radium therapy for malignant disease, great hope was entertained that the penetrative quality of these rays would enable them to destroy cancer cells beyond the reach of the surgeon's knife. High voltage and supervoltage machines were developed and have been employed with skill and courage but without improved results. Intracavitary radium has been implanted in a great variety of forms, and with the standardization of application, increasing numbers of milligram hours have been employed. While radiation therapy (x-ray and radium) has produced the highest survival rates of any method to date, these results are still far from satisfactory. Two-thirds of the women presenting themselves for treatment for carcinoma of the cervix still die within five years from extension of the carcinoma to the pelvic nodes and beyond with fatal sequelae.

Surgical lymphadenectomy, both combined with radiation therapy and alone, has been employed and found wanting. Recent efforts to carry radiant energy to the pelvic lymph nodes by the use of radioactive gold have been reported to offer some advantages.

The past several decades have witnessed considerable standardization of therapeutic schedules and the establishment of statistical comparisons of five-year survival rates. The results of these studies have been most valuable and have resulted in improving the survival rates from about 25 per cent to 35 per cent over the past twenty years. As valuable as these five-year statistical studies have been, they have not enhanced our knowledge of the effect of radiation on the metastases in pelvic lymph nodes. These metastases continue to be our nemesis in the management of this disease.

Before a satisfactory study of the effect of radiation on pelvic lymph nodes could be made, two fundamental developments were necessary, safe access to the node area by surgery, and reliable methods of quantitating the radiant energy delivered by the various modalities. While surgical lymphadenectomy has been possible for a number of years, the poor results from this procedure have discouraged its employment.

Radiation dosimetry of roentgens delivered from x-ray and intracavitary radium has only recently become available and standardized. The work of radiation physicists such as Quimby and Parker has established conversion factors for point and linear sources of radium. It is now possible to calculate "tissue" roentgens delivered by intracavitary radium (or other gamma radiation sources) to any point in the pelvis.

We now have available a method for calculating and delivering a known amount of radiant energy to the lateral pelvic lymph nodes from several sources, and for determining microscopically the effect of such radiation on the node. Also, methods for directly measuring radiation delivered to the bladder and rectum have recently been developed.

Standardization of radium treatment has greatly facilitated the clinical use of radium but has not provided the patient with the maximum radiation or protection available. The tendency to employ a fixed small amount of radium, usually 5,000 to 6,000 mg. hr., without regard to distance and distribution, has limited the effectiveness of radiation therapy. One mg. of radium in the vaginal fornix for one hour equals 1 mg. hr., but this has approximately six times the effect on the lateral pelvic lymph nodes as 1 mg. hr. obtained from 1 mg. of radium placed in the cervix for one hour and many hundred times the effective radiation that would obtain if the patient carried 1 mg. of radium in her pocket for one hour.

Admitting the inaccuracies of depth dose calculations, we believe it is meaningless to compare roentgens in air or milligram hours of radium delivered in a series of patients as it is to compare minutes of surgery. We are all familiar with the effect of obesity on our operating time, but we often overlook a similar deleterious effect on the penetration of radiant energy.

While the biological effect of roentgens from radium and x-ray may not be identical, and since no uniform conversion factor is available, these two sources of roentgens have been summated in this report.

Certain principles of radiobiology have been established that may be applied here. The isodose curves for x-ray for given physical factors and port size are known and similar isodose curves for varying foci of radium are now available. There is fair agreement on the minimum cancerocidal dose of radiation in roentgens for many cancers and the maximum tolerance figures for various tissues have likewise been determined.

We undertook to bring these various factors into focus in planning an integrated therapeutic schedule for patients coming for treatment of squamous-cell carcinoma of the cervix. These features may be summarized as follows (Table II):

a, A minimum of 10,000 and a maximum of 20,000 roentgens to the cervix and local lesion; b, a minimum of 5,500 roentgens to the lateral pelvic lymph node area; c, a maximum of 5,000 roentgens to the nearest rectal point (later reduced to 4,000); d, a maximum of 5,000 roentgens to the bladder (later reduced to 4,000); and e, any skin portal (100 to 150 cm.^{2}) dose not to exceed 3,300 roentgens or moderate vesiculation. These tolerance levels are based on fractionated daily treatments administered over a six weeks' period.

It was decided to abandon standardization of technique and seek standardization of quantity of radiant energy delivered to the local lesion and to the lateral pelvic lymph nodes. The major effect of the radium is on the cervix and local lesion, its effectiveness decreasing approximately with the square of the distance in centimeters. X-ray is used primarily to affect the lateral pelvic lymph nodes with the concentration of roentgens decreasing with the distance

from the skin portals. By integrating the isodose curves of x-ray and radium, fairly satisfactory distribution of roentgens can be obtained throughout the pelvis (Figs. 1 and 2).

In summary, this project was designed to deliver a controlled amount of radiation to the cervical carcinoma and the lateral pelvic lymph nodes, and to study the effect of such radiation on these tissues microscopically. It was hoped that such combined individualized radiation and surgical therapy would greatly augment our knowledge of the effect of irradiation on metastatic carcinoma and might offer these patients enhanced opportunities of cure.

We anticipated certain unpredictable complications from this type of investigation and treatment but hoped that by careful application of known radiobiological data we would avoid serious sequelae.

While these studies have not been in progress long enough to offer any indication of the effect of this plan of therapy on five-year survival, cure rate, or late radiation complications, much valuable information has been obtained regarding the effectiveness of the planned irradiation on pelvic lymph node carcinoma.

TABLE II. RADIOBIOLOGIC FACTORS (FROM THE LITERATURE)

Minimal cancerocidal dose, squamous-cell carcinoma	5,000-6,000 r*
Cervical dose (γr only)	10,000-20,000 r
Bladder tolerance	4,000-5,000 r
Rectal tolerance	3,000-4,000 r
Vaginal tolerance	15,000-18,000 r
Skin tolerance	2,500-3,500 r

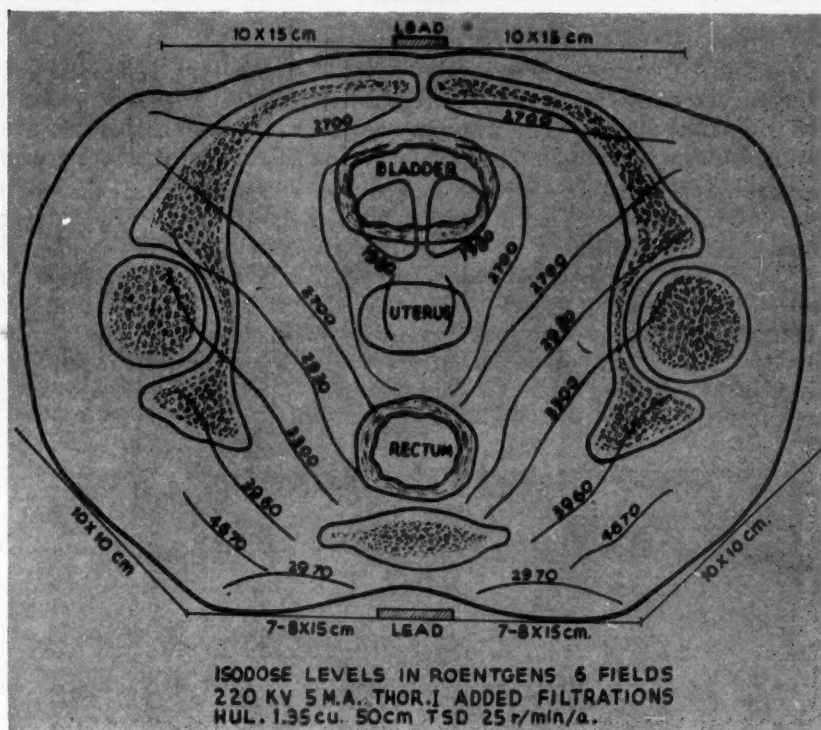REVISED DATA (DETERMINED FROM PRESENT STUDY)

	GAMMA ROENTGENS	X-RAY ROENTGENS	SUMMATION
Minimum cancerocidal dose (lateral pelvic wall)	1,500-2,000	3,500-4,000	5,000-6,000
Cervical dose	10,000-20,000	3,000	13,000-25,000
Bladder tolerance	4,000	1,500-2,000	5,500-6,000
Rectal tolerance	4,000	1,000-1,500	5,000-5,500
Vaginal tolerance	10,000-15,000	3,000	13,000-18,000
Skin tolerance 8 by 15 cm. port (220 kv. HVL 1.5 mm. cu.)	——	3,000-3,500	3,500

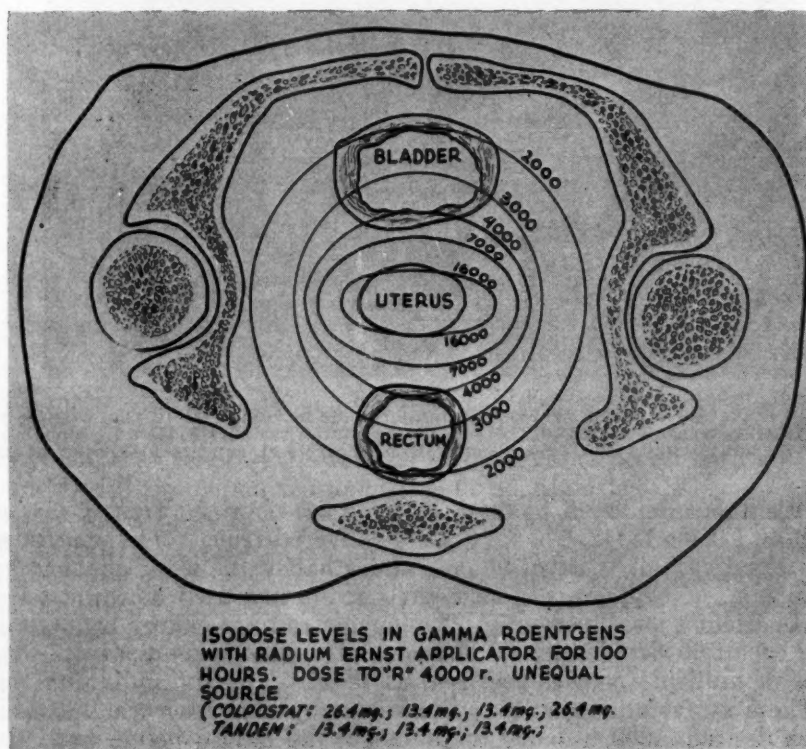*Summation of x-ray and gamma roentgens. Total radiation delivered in 5 to 6 weeks.

Plan of Study

The details of the plan for these patients are as follows. The clinical diagnosis of carcinoma of the cervix is confirmed by biopsy. The preliminary examination done in the out-patient clinic includes the usual history and physical examination, chest x-ray, pyelographic, proctoscopic, and cystoscopic examinations; laboratory work includes the usual hematologic and chemistry determinations together with urine analysis. The patient's physical condition is improved in so far as possible by transfusions, antibiotics, and other remedial procedures. In order to determine the distance from the skin and cervix to various points in the pelvis, the patient is measured by external calipers and by anteroposterior and lateral radiographs with a skin clip on the cervix (Fig. 3).

The patient is then seen in joint conference with the radiologists. Clinical staging according to the League of Nations Classification is determined by the

ISODOSE LEVELS IN ROENTGENS 6 FIELDS
220 KV 5 M.A. THOR.I ADDED FILTRATIONS
HUL. 1.35 cu. 50cm TSD 25 r/min/a.

A.

ISODOSE LEVELS IN GAMMA ROENTGENS
WITH RADIUM ERNST APPLICATOR FOR 100
HOURS. DOSE TO"R" 4000 r. UNEQUAL
SOURCE
(COLPOSTAT: 26.4 mg.; 13.4 mg., 13.4 mg.; 26.4 mg.
TANDEM: 13.4 mg.; 13.4 mg.; 13.4 mg.;)

B.

Fig. 1.—Isodose curves of x-ray, *A*, and radium, *B*, indicating the factors employed.

group. A plan of treatment is formulated that will deliver 10,000-20,000 roentgens to the cervix and 5,000-6,000 roentgens to the lateral pelvic nodes (ischial spines) as indicated above. The number and location of skin portals are determined and in general the amount and distribution of the radium foci are planned.

In general, early lesions (League I) are treated by an initial dose of radium (about one-half of the total) followed by two-thirds of the x-ray, the balance of the radium, and the balance of the x-ray in continuous daily fractionated (Coutard) treatments. Surgery is carried out relatively soon in these patients. In the more advanced lesions, x-ray is employed first with a single application of radium being implanted about halfway or two-thirds of the way through the x-ray schedule. In this experimental project surgery followed the completion of the irradiation at varying intervals to study the effect of the irradiation on the lymph nodes and parametrial tissues.
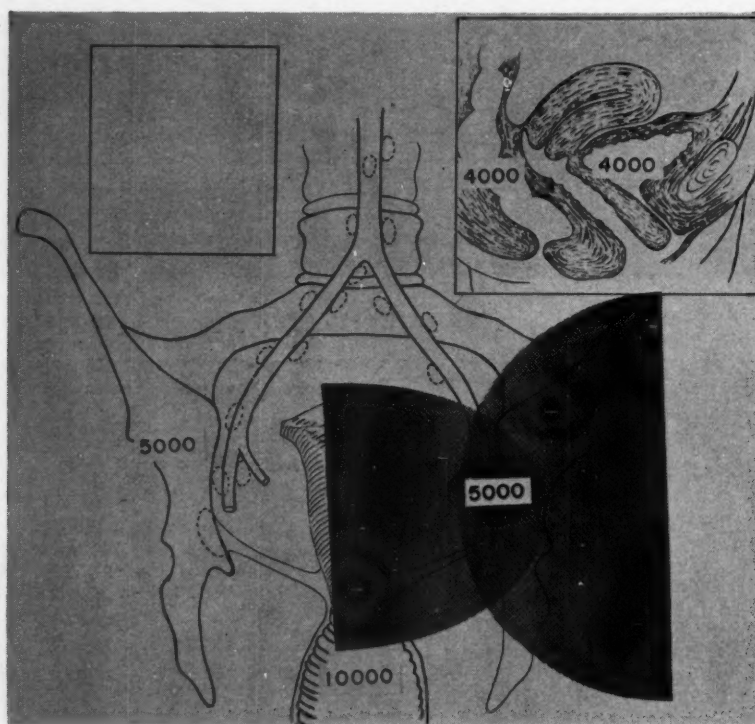

Fig. 2.—Diagram showing amount of radiation to be delivered to the various points in the pelvis from x-ray and radium. The summation of the two fields of radiation effect at the lateral pelvic wall permits the development of a theoretical cancerocidal dose of radiation.

The roentgens delivered to these patients are obtained from x-ray, radium, and cobalt 60 (Table III). The x-rays are delivered from 220 kv. machines using 15 Ma., a target skin distance of 50 cm., and a half-value layer equal to approximately 1.5 mm. of copper. Six to eight portals are used as indicated by the individual patient's measurements. The gamma radiant energy is obtained from radium or cobalt 60 shielded by 1.0 mm. of platinum or its equivalent. An Ernst applicator or multiple needles are used as required by the individual patient's lesion. These x-rays and gamma rays are employed in such combinations as to deliver the desired 5,000 to 6,000 roentgens to the lateral pelvic wall, 10,000 or more roentgens to the cervix and less than 4,000 roentgens to the rectum and bladder (summating the gamma roentgens and x-ray roentgens directly) (Fig. 2, Table II). For purposes of comparison the number of milligram hours of

radium or millicurie hours of cobalt 60 vary considerably and range from 6,000 to 10,000 mg. hr. of radium or 4,000-6,000 mc. hr. of cobalt 60.

The final calculation of radiation delivered to the various points in the pelvis is determined from external measurements and from anteroposterior and lateral six-foot teleroentgenograms taken immediately after insertion of the intracavitary applicator. The external os and the farthest margin of the cervix (when possible) are identified with skin clips. The inner margins of the acetabuli are easily visualized for the calculation of roentgens delivered to the lateral pelvic nodes. The bladder and rectum are identified by contrast media so that the roentgens delivered to them can be calculated. By these means it is possible to identify and measure the distances from the various sources of rays to the points of interest (Fig. 4). By the use of converted Quimby Tables, the roentgens delivered to any and all points in the pelvis can be determined by calculation.

Fig. 3.—Anteroposterior film of pelvis with skin clip on each margin of cervix. This type of film is used to calculate the distance from radium foci to the lateral pelvic wall.

Occasionally, the radium (or cobalt) may be found unduly close to the rectum or bladder or an otherwise unfavorable application is seen on the film, and it is possible to reapply the radium at once with special care and packing to offer additional protection without loss of full radiation.

At intervals varying from 2 to 12 months following the completion of radiation, the patient is operated on, and a Wertheim hysterectomy with extensive gland dissection is done when possible. In advanced cases a biopsy of the cervix with pelvic lymphadenectomy is combined with palliative procedures such as hypogastric artery ligation, sympathectomy, etc.

This report is based on the microscopic analysis of the lymph nodes and other tissue specimens removed at operation.

Results

Forty-two cases were managed by this schedule and complete information is available on 24. Table IV shows the statistical data regarding these women.

TABLE III.   RADIATION FACTORS

X-ray.—
    Kilovoltage   220 kv.-15 Ma.

Kilovoltage	220 kv.-15 Ma.
Target skin distance	50 cm.
Half value layer	1.5 mm. cu.
Port size	10 × 10 cm.
	10 × 15 cm.

Protection of rectum and bladder, 2 cm. strip lead in midline (present
    use 4 cm.)
Focal point of several ports at lateral pelvic wall

Radium.—

Ernst applicator with 5 to 7 foci	
Filter-platinum equivalent	1.5 mm.

Cobalt.—

A. E. C. Cobalt 60	
Filter-platinum equivalent	0.6 mm.
Modified Ernst applicator with 7 to 9 foci	
Interstitial needles (4-6 cm. active length)	0.5 mc./cm.

TABLE IV.   GENERAL DATA

Age.—

Average	46 years
Range	23-67 years

Stage.—

Stage I	6
Stage II	14
Stage III	4

Radiation, Surgical Interval.—

Average	6 months
Range	2 months – 13 months
Under 3 months	6
3 to 6 months	8
Over 6 months	10

Roentgens Delivered.—
  Cervix:

Average	16,576
Range	9,146 – 27,943
Under 10,000	1
10,000 – 15,000	10
15,000 – 20,000	7
Over 20,000	6

  Lateral Pelvic Wall:

Average (right 5,750 – left 5,713)	5,731
Range	3,555 – 7,742

  Bladder:

Average	3,475
Range	1,000 – 6,016

  Rectum:

Average	3,621
Range	1,470 – 6,109

There were 6 patients in Stage I, 14 in Stage II, and 4 in Stage III. Their aver-
age age was 46 years, with the youngest being 23 and the oldest 67. The interval
between completion of radiation and surgery averaged 6.5 months, with 6 under
three months, 9 between three and six months, and 9 over six months. These
longer intervals were permitted to ascertain the late effects of radiation and to
permit a reasonable opportunity for recurrence if any residual viable cancer
remained. The average "tissue" roentgens delivered to the cervix was 16,744
with a range of 9,146 to 27,943; the lateral pelvic wall received an average of
5,839 roentgens with a range of 3,555 to 7,742; the bladder from 1,000 to 6,016;
and the rectum from 1,470 to 6,109 roentgens. The individual protocols are
listed in Table V.

Such an intensive treatment program was designed to eradicate the cancer
if possible.   When the bladder and/or rectum were already involved the possi-
bility of fistulas was accepted, with reliance on future reconstructive surgery to
restore function in so far as possible.   Such was the case in A. C. who had a Stage
III (or IV) lesion with involvement of the rectovaginal and vesicovaginal septa.
Intensive therapy destroyed all microscopic evidence of carcinoma but left the

A.

B.

Fig. 4.—Anteroposterior, *A*, and lateral, *B*, films of pelvis with Ernst applicator in place.
The skin clips mark the margin of the cervix and the extent of the tumor in the vagina.   The
balloon on the Foley catheter is filled with sodium iodide and the rectum is identified with
barium paste.   These films are taken immediately on placing of the radium and permit cal-
culation of roentgens to be delivered per hour to each point in the pelvis.

TABLE V.

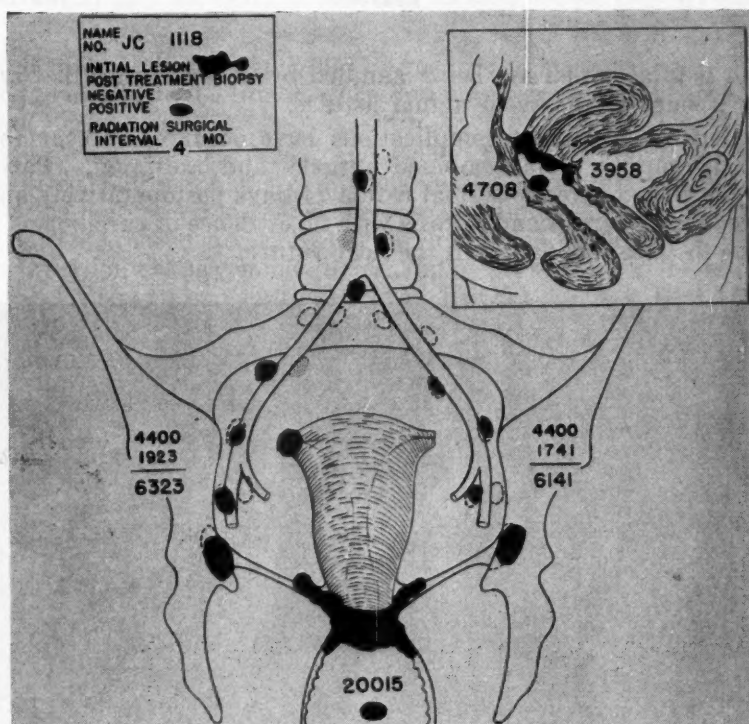| NAME	AGE (YEARS)	STAGE	RADIATION SURGERY INTERVAL MO.	RADIATION					POSTRADIATION THERAPY			COMPLICATIONS
				BLADDER	RECTUM	CERVIX	LATERAL PELVIC WALL		CERVIX	L.P.W.	OTHERS	
							RIGHT	LEFT				
V. B.	49	III	7	2,124	4,000	10,057	4,756	4,756	+	+	+	Iliac and aortic nodes
E. B.	60	III	5	1,175	2,933	18,000	5,592	5,923	0	0	0	
A. C.	41	III	9	3,917	3,917	15,000	5,542	7,742	0	0	0	Pretreatment involvement rectum and bladder fistulas
F. C.	33	I	10	1,541	1,470	14,178	6,011	6,011	0	0	0	Incomplete node dissection
J. C.	33	II	3	5,004	3,796	27,943	6,659	6,659	0	?	?	
J. C.	30	II	4	3,958	4,708	20,015	6,323	6,141	+	+	+	Hypogastric node
L. D.	29	I	2	2,996	2,432	22,113	4,392	4,009	0	0	0	
V. D.	41	II	13		6,109	9,146	5,504	3,804	0	+	0	Irradiation fistulas
J. E.	44	II	3	4,947	4,000	14,769	5,382	5,382	0	0	0	
L. F.	57	II	10	4,000		10,281	5,931	3,555	0	0	0	Severe proctitis and cystitis
N. G.	51	II	11	4,457	5,695	20,090	6,071	6,071	0	0	+	Postoperative gangrene and death Pulmonary metastasis
I. H.	45	II	4	2,374	3,094	12,762	5,495	5,829	0	+	0	Obturator
L. H.	44	III	5	3,426	4,519	18,000	6,363	6,363	0	0	+	Severe proctitis Aortic node
C. M.	51	II	5	3,400	2,945	14,984	6,503	6,503	0	0	0	Ischiorectal abscess
M. Me.	53	II	9	3,874	3,360	17,053	6,382	6,382	0	0	0	Proctitis Neg. Biopsy
T. O.	59	II	8		—	10,195	6,194	6,194	+	+	+	Entire pelvic nodes and viscera
J. P.	55	II	5	4,614	4,000	15,376	6,348	6,371	0	0	0	Proctitis
H. R.	67	II	3	4,000	2,738	22,714	5,226	5,226	0	0	0	Previous hysterectomy
N. R.	23	I	3	3,250	2,850	15,000	4,560	5,620	0	0	0	Proctitis
N. S.	57	I	8	6,016	3,909	18,000	5,615	6,430	0	0	0	Proctitis with ulcer
B. T.	41	II	5	1,000	3,347	14,551	4,548	4,548	0	0	0	
E. T.	50	I	6	4,680	4,128	15,193	6,540	6,540	0	0	+	Uterine horn Aortic node
B. W.	37	I	2	2,998	3,000	24,419	6,400	6,400	0	0	0	Previous hysterectomy
M. W.	62	II	8	2,715	2,715	18,000	5,671	5,671	0	0	0	

Fig. 5.—Patient, J. C.   Diagram to illustrate the roentgens delivered by x-ray and radium to various points in the pelvis.   This patient had residual carcinoma in the cervix despite 20,000 r.
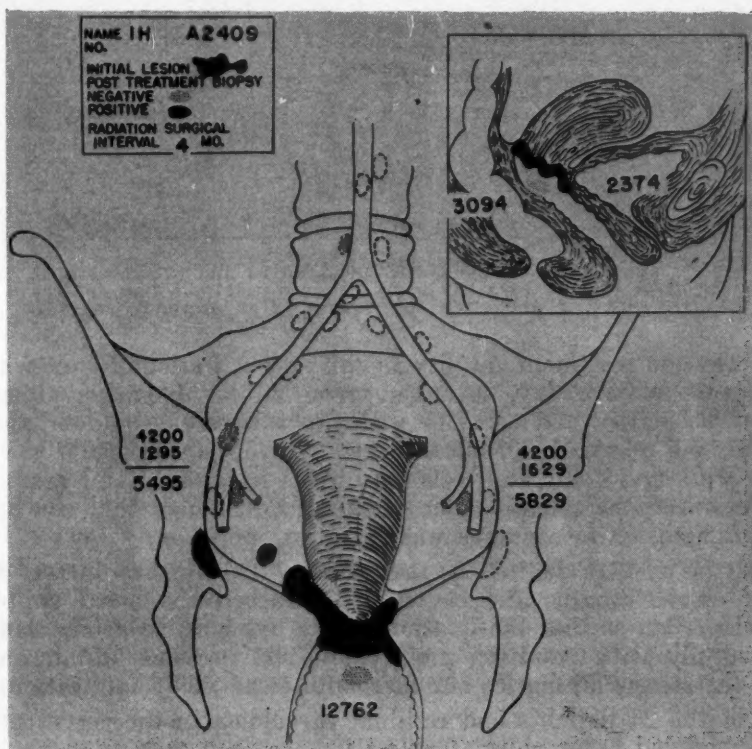

Fig. 6.—Patient, I. H.   Diagram of roentgens from x-ray and radium delivered to various points in the pelvis.   Twelve thousand roentgens eradicated the carcinoma from the cervix but 5,000 r. failed at the lateral pelvic wall.

patient with fistulas which are being handled by ureteral-intestinal anastomosis and a later closure of the rectovaginal fistulas.

Certain direct treatment complications have occurred, presumably due to loss of bloody supply from combined surgery and radiation. Patient J. E. (Stage II) developed a vesicovaginal fistula 24 days postoperatively and biopsies have revealed only necrosis and fibrosis with no evidence of carcinoma. Attempts will be made to close this fistula in the near future.

Fig. 7.—Silver clips placed on the aortic, hypogastric, and obturator node areas. Black lines indicate the areas covered by x-ray ports. Hypogastric and iliac nodes are just within the field of effective radiation and often do not receive an adequate summated dosage.

There was one treatment fatality in this series, Patient N. G., who died on her tenth postoperative day. Autopsy revealed an extensive phlegmon and gangrene of the entire pelvic cavity with necrosis of the bladder and ureters. This patient had received 20,090 roentgens to the cervix, 6,071 roentgens to each pelvic wall, and 4,457 and 6,695 roentgens to bladder and rectum, respectively. Eleven months elapsed prior to surgery, at which time the hypogastric artery was ligated. No carcinoma was found at operation.

It is our belief that the intense radiation incited a dense fibrosis during the intervening eleven months and severely diminished the blood supply to the bladder and ureters so that the ligation of the hypogastric artery compromised the blood supply with resulting gangrene. The presence of an unsuspected pulmonary metastasis minimizes our discomfiture at this complication.

Three of the 24 patients had residual carcinoma in the cervix at the time they were scheduled for surgery (Table VI). In each case extensive carcinoma was found throughout the pelvis (Patients V. B., T. O., J. C.). These patients

had received 10,057, 10,195, and 20,015 roentgens, respectively, to the cervix which failed to eradicate the tumor. These tumors were apparently radioresistant (Fig. 5 and Fig. 8).

In three instances, I. H., V. D., and B. T. (Table VI and Fig. 6) the cervix became negative, but there was carcinoma in the upper pelvis which appeared active. At this point we questioned the upward limits of radiation therapy and on several patients placed silver clips at the site of the aortic nodes, the subaortic area, the bifurcation of the common iliacs, and at the obturator fossae. By superimposing the skin portals over these films (Fig. 7), we saw that the iliac and
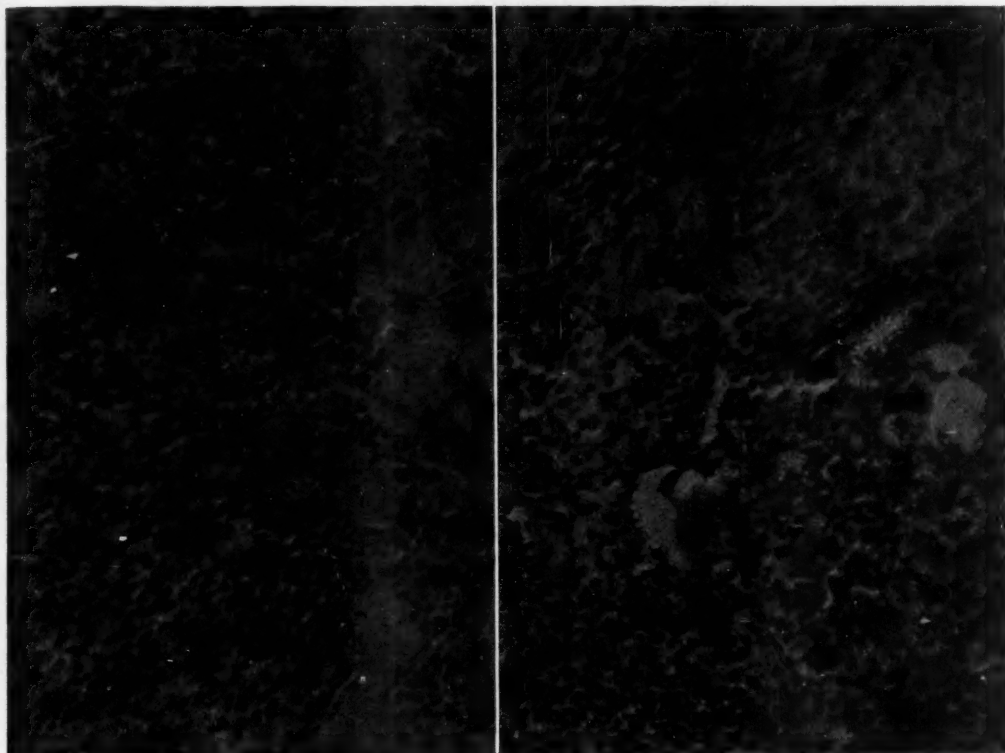

Fig. 8A.—Pelvic lymph nodes from Patients N. G., left, and I. H., right, showing effect of irradiation. Note hyalinization, amyloid deposit, and destruction of follicles obtained from 5,500 to 6,000 r.

subaortic nodes were just within the field of x-ray and were probably too distant to receive an adequate combined dosage of radiation. The hypogastric and obturator nodes appeared to be within the area of adequate radiation. It is possible that the residual carcinoma found in these women whose local lesion had disappeared could have been due to the falling off of radiation at the outer margins of the fields.

In Patient I. H., the cervix and paracervical tissues were negative and an obturator node was positive. The cervix in this woman received 12,762 roentgens and the obturator node 5,495 roentgens. Whether the survival of this carcinoma in the lymph node represents some mystical "protection" or is the result of the differential in radiation cannot be determined. A similar situation obtained in Patient, B. T.
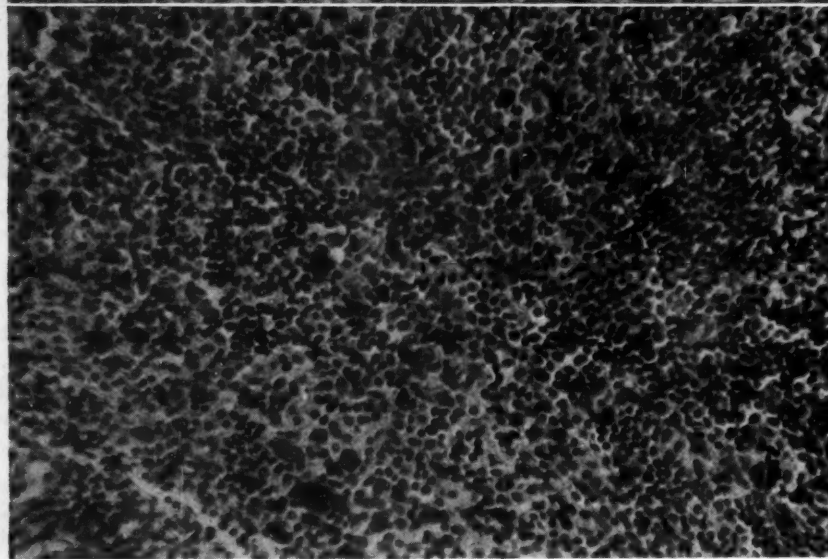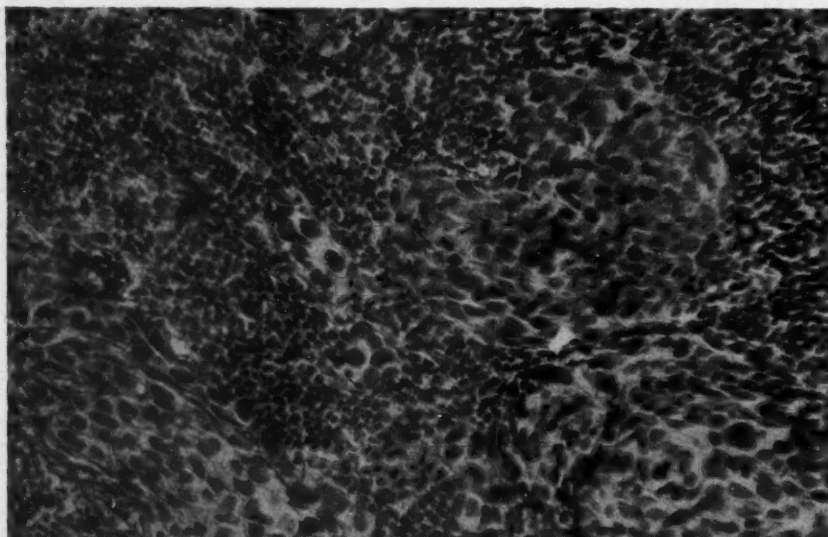
In the other 18 women, the cervix became negative and no living carcinoma could be found at operation in the pelvic lymph nodes or parametrial tissue

TABLE VI. POSTRADIATION BIOPSY RESULTS

Positive cervix, positive pelvic nodes		3
Stage II (J. C. and T. O.)	2	
Stage III (V. B.)	1	
Negative cervix, positive pelvic nodes		3
Stage II (I. H., V. D., and B. T.)	3	
Negative cervix, negative pelvis		18*
Stage I	6	
Stage II	9	
Stage III	3	

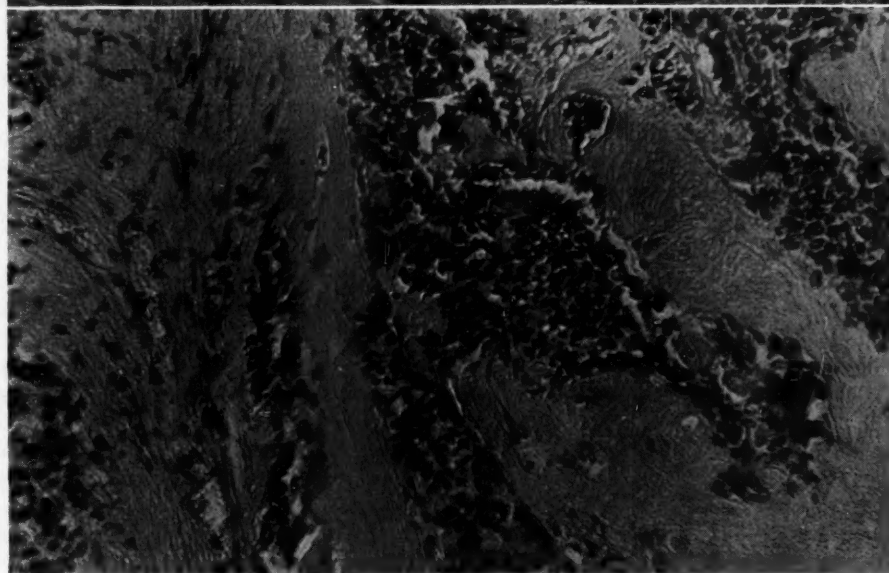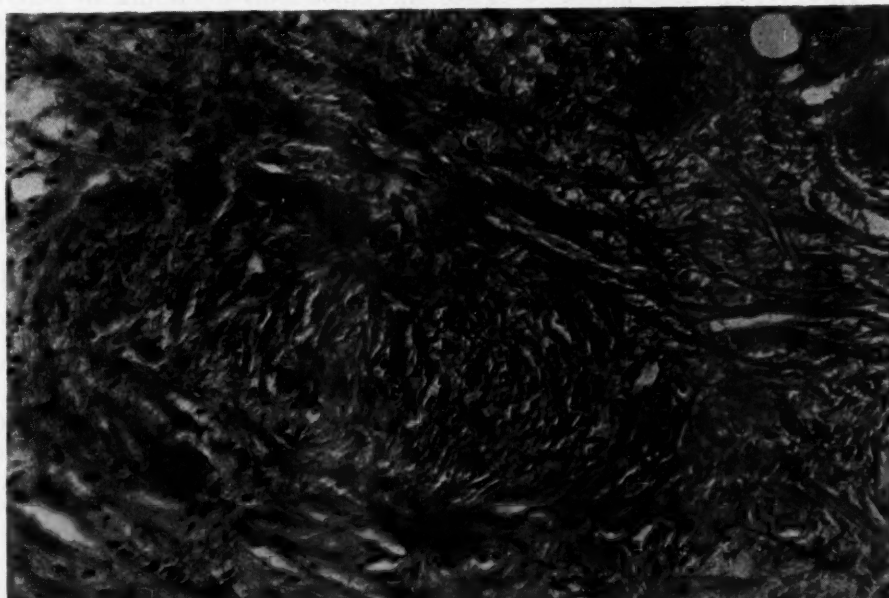*Patients N. G. and L. H., extrapelvic metastase.

B.

C.

Fig. 8B.—Aortic node from Patient L. H., showing metastatic carcinoma infiltrating the node. This area was not irradiated.

Fig. 8C.—Pelvic lymph node from Patient V. B., showing bizarre changes in atypical cells which are probably radiation changes in carcinoma. This node received about 4,700 r.

(Table VI).   All pelvic nodes showed extensive evidence of irradiation effect with areas of hyalinization and focal necrosis, some of which are suggestive of a possible previous metastasis which had disappeared (Table V and Fig. 8).

All are familiar with the difficulties encountered in attempting to read metastasis in lymph nodes, particularly irradiated nodes.   Yet the reading of these slides by several members of the Department of Pathology failed to estab-

D.

E.

Fig. 8D.—Paracervical tissue from Patient N. G., showing extensive necrosis of connective tissue.   This area received about 7,000 r from x-ray and radium.

Fig. 8E.—Biopsy of cervix of Patient V. B., seven months after 10,000 r showing necrosis of stroma but active carcinoma persisting.

lish the presence of surviving carcinoma in the lymph nodes or parametrial tissue of these women. On the basis of the figures of Taussig, Morton, Nathanson, Henriksen, and Meigs, 20 to 30 per cent of the nodes might have been involved. Our failure to find residual carcinoma is of interest and perhaps significant.

Comment

Whether this intensive individualized treatment schedule will greatly increase the serious sequelae or improve our survival rates cannot be determined at this time. However, it does appear possible in radiosensitive tumors to deliver a cancerocidal dose of radiation throughout the pelvis by these techniques described.

To provide such cancerocidal dosage requires the use of maximum tolerable radiation. The usual protection offered by the small safe 5,000-6,000 mg. hr. of radium does not offer the maximum benefit of radiation therapy to each patient. By employing the visceral protection offered through these techniques, large amounts of radiation can be safely administered.

These studies have not advanced far enough to offer definite conclusions regarding previously suggested tissue tolerances. However, in the light of this experience, it seems wise to lower maximum bladder and rectal dose to 3,500-4,000 r. rather than 5,000 suggested by Todd (Table II).

Certain tumors were found to be resistant to 20,000 r. In two instances, carcinoma survived 10,000 r. and in one patient 20,000 r. but no residual cervical carcinoma has been found in patients receiving over 21,000 r.

In all instances where the cervical lesion disappeared and the lateral pelvic wall received over 5,500 r. no residual carcinoma was found. In two cases, even though the cervix became negative, nodal carcinoma was found despite 4,000-5,000 r. delivered to the lateral pelvic wall. These findings suggest that a summated 5,000-6,000 r. is a minimal cancerocidal dose at the lateral pelvic wall (Table II).

Certain comments on the optimum intervals for surgery are suggested by these studies. We permitted varying intervals up to one year to elapse following radiation prior to surgical exploration. This was done both to permit any possible recurrence or residual in the nodes to become obvious, and also to study the effect of radiation on these tissues at varying intervals.

The fibrosis from this intense irradiation does not become significant until after three months. After this time tissue fibrosis progressively fixes the pelvis and renders surgical dissection increasingly more difficult. The fatality and most of the serious postoperative complications have occurred in the group operated on after six months.

In most of these cases, hypogastric artery ligation has been used to reduce the blood loss in these extensive dissections. It is our impression that irradiation endarteritis and fibrosis extending over 6 to 9 months combined with artery ligation critically reduce the blood supply to the pelvis and compromise the postoperative healing and convalescence. This was probably the cause of the fatality in C. G.

If postradiation surgical extirpation is to be included in the treatment of carcinoma of the cervix, it is our opinion that it should not be delayed more than 2 to 3 months.

Late complications of this combined radiation-surgical therapy cannot be anticipated at this time. Undoubtedly, complications will appear which will require additional care and may serve to guide our further studies and treatment.

Addendum

When this paper was written it was anticipated that complications might develop later. At the time of publication (6 to 18 months post treatment) certain complications have appeared

that should be appended in this report. Several of the patients reported above have developed complications within the pelvis similar to those described in cases N. G. and J. E. This has involved ureteral obstruction, tissue necrosis, and fistulation. In each instance the time from radiation to surgery was more than four months and the surgical dissection was extensive including bilateral hypogastric artery ligation and complete pelvic lymphadenectomy.

In addition to the 24 fully studied cases reported above, there have been 49 additional cases treated by radiation only with the use of the same technique. Of these, 38 are four or more months post treatment at this time, and only two have developed complications which might even remotely be attributed to the radiation treatment.

It would appear, therefore, that the high incidence of complications in the series reported in this paper is due to the superimposed surgical attack on intensively irradiated tissues, so compromising the blood supply that fibrotic and ischemic complications appeared.

This study is continuing but in the light of these problems the surgical procedure is being limited to pelvic lymphadenectomy.

Summary

This series of 24 cases is not large enough to permit any final conclusions, but the detailed study of these cases seems to throw considerable light on the problem of irradiation therapy of carcinoma of the cervix.

Many advantages have accrued from this project which is still continuing; one of the most significant has been the improved understanding of the treatment (both surgical and radiological) of cancer of the cervix by the house staff of both departments. Also, a greatly enhanced mutual respect has been developed between radiologists and gynecologists as they plan together the treatment for an individual patient.

The following statements seem justified from this study:

1. Five thousand to 6,000 "tissue roentgens" seems to be the minimal concentration of radiation that will eradicate carcinoma in the pelvic lymph nodes in radiosensitive tumors, when delivered in 5 to 6 weeks.

2. By the integration of all avenues and modalities of radiation therapy, a minimum of 5,000 to 6,000 r. can be delivered to all areas of the deep pelvis with apparently minimal risk to normal viscera.

3. Certain tumors have been shown to be radioresistant even with 2 to 3 times the usual cancerocidal dose of roentgens; 20,000 r. failed to eradicate the tumor in one instance.

4. If surgery is employed postradiation, it should be done relatively early (2 to 3 months) before collateral circulation is seriously compromised.

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Discussion

DR. R. GORDON DOUGLAS, New York, N. Y.—Dr. Brown has attacked courageously one of the most difficult current problems confronting oncologists, radiologists, and gynecologists in attempting to determine the therapeutic effect of radiation on lymph nodes involved with squamous-cell carcinoma. Pathologists have long had difficulty in interpreting the significance of apparently viable tumor cells in axillary lymph nodes long after removal of the primary lesion and radiation therapy. Microscopically such tumor cells may appear viable; however, obliteration of lymphatic channels by fibrosis, partial destruction of the tumor cells and the diminution of blood supply may all tend to limit the activity and spread of these cells. It is quite possible that under such conditions tumor cells may actually exist for many years without deleterious effect on the patient. Some cells may be rendered definitely nonviable, commonly designated as ghost cells, and others appear to be most certainly viable. Between these extremes there is a group in which the cells are probably affected to some extent by the radiation but whether they are actually viable or not may be impossible for the pathologist to determine. Accordingly, it becomes extraordinarily important to accumulate all possible information concerning the potentialities of apparently viable cancer cells in a lymph node.

The liaison that Dr. Brown and his associates have established between the radiologist and the gynecologist is to be commended in the very highest terms. The emphasis on tissue dosage rather than on the amount of x-ray delivered in air or the statement of milligram hours of radium employed represents a highly scientific approach to the radiation problem. It is essential in calculating dosages obtained by radium techniques that they be interpreted in roentgens. While there may be some error in summating gamma irradiation with x-ray irradiation the error is not large and certainly it is vastly superior to referring to the total x-ray irradiation in terms of roentgens and radium dosage calculated in terms of milligram hours. Reporting radium treatment in terms of milligram hours is mathematically and clinically meaningless. It might well be compared to reporting x-ray treatments in terms of minutes of exposure. The following factors modify radium dosage in roentgens: the milligrams of radium employed, the hours of exposure, the filtration of platinum and other materials, the dimensions of the sources, and the distance from various sources to the region receiving treatment. One is impressed with the accuracy with which the author has determined the dosage of the x-ray therapy in roentgens to various points in the pelvis and the definitive manner in which the radium has been placed in the uterus.

Of his total material, namely 24 patients, 80 per cent had all known tumor destroyed by the radiation therapy and in only 3 patients was there any viable tumor found in the cervix. One might argue that 80 per cent of these 24 patients did not need surgery and, in effect, the 24 were operated upon in order to detect and treat the 5, or 20 per cent, of patients who had persistent and apparently viable tumor. One must conclude that this latter group of patients had a more resistant form of carcinoma than the others in that apparently the extent of their disease was no more than in those patients in whom the tumor was not found in the tissues removed. Moreover, the location of the persistent nodes in the 5 patients with lymph node involvement was at the usual sites in the pelvis. Dr. Brown and his associates would then appear to be justified in their conclusion that they have, by integrating all modalities of administration of irradiation, delivered 5,000-6,000 r. deep in the pelvis, which apparently will eradicate radiosensitive carcinoma. It may be that it is not necessary to deliver such a high dosage in many instances where the tumor is very sensitive. We have an example of that in a patient in our institution at this time who is quite obese and had, accordingly, a calculated tissue dose at point ''B'' in the pelvis of 3,500 r. and 6,000 r. by vaginal cone delivered directly to the tumor. Pathologic examination of all lymph nodes following operation eight weeks after completion of radiation was negative for carcinoma and the cervix failed to reveal the presence of tumor. The original lesion at the time of the initiation of therapy was 6 cm. in diameter with complete destruction of the cervix and early crater formation.

A patient operated upon two months after completion of x-ray therapy revealed positive right external iliac node rather high up on the vessel. A high-power view of this showed very little radiation effect. However, a portion of the right obturator node from the same patient displayed considerable fibrosis, infiltration of fat, and no evidence of viable tumor. A high-power view showed fibrosis, hyalinization, and nonviable ''ghostlike'' cells. This case illustrates a cancerocidal dose in the obturator region calculated at 3,900 r. while nearer the periphery of the radiation field no significant change is illustrated.

One must take into consideration in the interpretation of these tissues that complete radiation changes have not as yet taken place because of the lapse of only two months following the completion of radiation.

It has been our experience that patients treated by radiation and subsequent operation may develop later rather extensive fibrosis. This often is represented by a broad shelf of induration extending from the perirectal areas to the lateral pelvic wall. I would like to ask Dr. Brown if he has had a similar experience.

DR. JOE V. MEIGS, Boston, Mass.—I think this paper is unusually good and is the sort of thing all of us should be interested in. My personal opinion is that we are far behind in our evaluation of radiation. We, in this country, who are interested in cervical cancer, have a surgical and millicurie and milligram base line but do not have a gamma roentgen base. We are now sending men to Europe because we must know what we can expect with radiation of the newer type.

DR. WILLARD M. ALLEN, St. Louis, Mo.—Successful treatment of carcinoma of the cervix is dependent on adequate management of the parametrium and the lymph nodes. We have approached this with the same motives as Dr. Brown but in a different manner.

In the past year and a half we have treated 25 patients with Stage O and Stage I carcinoma of the cervix by injecting radio active colloidal gold into the parametrium prior to radical hysterectomy and excision of pelvic lymph nodes. Gold is an inert element that can be readily injected in liquid solution into the parametrium. Ten per cent of the radiation is due to gamma rays and 90 per cent is due to beta rays. The operation we have been doing is about as radical as that described by Dr. Meigs. The main question is, how much irradiation is obtained? In the past two months we have determined this with some accuracy. A scintillation counter is placed in the pelvic cavity at the time of operation to get an estimate of gamma radiation. With this counter placed on the inner side of the symphysis we get 2,000 gamma r. and in the obturator area we get 3,000 gamma r. That is only 10 per cent of the total radiation so we are giving fairly intensive radiation. The gold is picked up by phagocytes and is found in the lymph channels and in the lymph nodes. Here then is a radioactive agent which travels along the same channels as the tumor cells and hence produces maximal irradiation in the most important areas. We have had in this series of 25 patients three who have had invasion of either the parametrium or the lymph nodes. In these three patients the tumor cells seemed devitalized and the patients are still alive and well.

DR. BROWN (Closing).—I am very appreciative of the kind discussion accorded this report. I would like to state that the surgery in these patients was done as an experimental procedure to get the necessary tissue for the study. What the final role of surgery will be is impossible to state now.

This study suggests that whenever carcinoma of the cervix was eradicated and the lateral pelvic walls received 5,500 r., no viable carcinoma was found. It is possible that some of the cancerous metastases could have been eliminated with less, but in this series, when we were able to get a theoretical cancerocidal dose of radiant energy to the node bearing area, it did the job.

PREVENTION OF THROMBOSIS AND EMBOLISM IN GYNECOLOGICAL SURGERY*

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PULMONARY embolism is a major tragedy. Although it occurs in both non-surgical and surgical patients, the accident seems more tragic when it appears in the latter group. In the welter of literature dealing with thrombosis and embolism almost every phase of the subject has been discussed. Much that has been written is controversial, but improvement in the diagnosis and treatment cannot be denied. When emboli have been transported from their source, treatment is of little avail. The prospect of preventing the precursors of embolism, phlebothrombosis and thrombophlebitis, has more to offer. The possibility of prevention deserves careful consideration and has not been duly emphasized.

Venous thrombosis arises in a diversity of situations, and, like many other biologic processes, multiple factors are involved. Circulatory retardation has long been recognized as a prime factor in thrombosis. A brief reference to the physiology of venous circulation will serve as a basis for explaining how the normal relations may be disturbed by the circumstances attending the operation. Although injury to veins and chemistry of blood are important to the process of thrombosis, they have been omitted intentionally in order to focus attention on the role of venous stasis.

The fatal emboli occurring in the gynecological department of the Henry Ford Hospital since the inception of the department in 1926 have been studied individually at the time of occurrence. More recently the group has been reviewed as a whole.

The incidence of fatal emboli for the past 24 years was 23 in 17,742 patients on whom operations were performed. The writers had five (Pratt 3, Hodgkinson 2) of these cases of fatal emboli for which pertinent data are presented here.

Case Reports

CASE 1.—C. P., No. 94233, was a white woman, aged 36 years. She had been pregnant twice with one miscarriage. She was a saleswoman in a department store and was burdened with the prolonged care of a father who died of carcinoma, and with financial worries about her mother. Over a period of years she had had numerous headaches. The history was otherwise negative, except for the local condition, pain in the left side of the pelvis. At the time of operation on April 5, 1930, an inclusion cyst of the vaginal wall was removed, supravaginal

hysterectomy, left salpingo-oophorectomy and appendectomy were performed for fibromyomas of the uterus and a chronic salpingitis. For sedation, morphine was given preoperatively and postoperatively. Sedation was heavy. The wound healed satisfactorily. During her postoperative course she maintained a rapid pulse and elevation of temperature until the day of discharge, the fifteenth day. The patient was re-admitted to the Medical Service three days later with a temperature of 102° F., pulse 120, and white blood count 19,000. There was x-ray evidence of bronchopneumonia. The clinical diagnosis was pneumonia and pulmonary emboli. The patient died on April 27, 1930, twenty-two days after operation. No autopsy was permitted, but the clinical impression was that death occurred from pulmonary embolus and/or pneumonia. The source of the embolus was thought to be phlebitis in the pelvic veins. Had antibiotics been available the infection could have been expected to respond. With the newer means of therapy this embolus might have been prevented.

CASE 2.—E. Y., No. 218555, was a white widow, aged 53 years, who had two children. Her admission complaint was uterine bleeding. A diagnosis of fibroid tumors had been made by her physician in Nebraska who had advised surgery. The patient came to this hospital for the purpose of operation. She was seen only once preoperatively. Her hemoglobin was 12.3 Gm. and red blood count was 5,130,000. The preoperative sedation consisted of Sodium Amytal, grains 3, the night before operation, Sodium Amytal, grains 6, at 6:30 on the morning of operation, and Sodium Amytal, grains 3, when she was sent to the operating room. At the time of operation on June 22, 1935, a complete hysterectomy, salpingo-oophorectomy, and appendectomy were performed. Exploration of the abdomen showed gall stones in the gall bladder. There was no postoperative shock. She received morphine, codeine, and Nembutal postoperatively. The day after operation her temperature rose to 100.2° F. and her pulse was 110. The temperature and pulse receded to normal by the fourth day. The patient seemed to be doing well postoperatively, but died suddenly June 26, 1935, on the fourth postoperative day. Permission for autopsy was granted by telegram, but was obtained too late to permit an autopsy before the time the body had been promised to the undertaker. The clinical evidence indicated pulmonary embolus. At the time the patient was seen preoperatively the emotional background was not carefully evaluated. The sedation was unduly heavy. Otherwise nothing extraordinary was noted in this patient's course in the hospital.

CASE 3.—L. T., No. 361665, a white woman, aged 59 years, was treated for pyelitis in 1942 and 1946. In 1947, her sister died of cancer. This affected her profoundly and she never felt well after that. She tired easily and was depressed and had a great fear of cancer. She had a slight pinkish vaginal discharge. Papanicolaou smears were negative. Since she had been advised for several years to have a repair of cystocele and rectocele she was now advised to have a vaginal hysterectomy and repair. This was done on Feb. 27, 1948. The pathological examination revealed early adenocarcinoma of the uterus. Her postoperative convalescence was uneventful. She was discharged on the thirteenth postoperative day, but advised to have treatment for varicose veins later. She did not return for examination and did not respond to recall letters until Nov. 7, 1949. At that time she mentioned a lump in her breast which had been present for nine months. She was found to have a carcinoma and an operation was advised. She wanted to think it over. In spite of follow-up letters, she did not return until March 16, 1950. A radical mastectomy was performed on March 20, 1950. She was inclined to be belligerent and uncooperative throughout, and emphasized that she was unduly urged to have an operation. Pulse rate increased throughout her postoperative course. Her temperature varied, but averaged about 100° F. No definite focus of infection was demonstrated. Penicillin was given without appreciably affecting the temperature. Her legs were repeatedly examined and not found to be tender. The patient was at times apathetic, cooperated poorly, ate scantily, and complained of weakness. Three days before she died there was a striking change in her mental attitude with great apprehension. Although she was thoroughly examined no definite cause for the change was found. She died suddenly of pulmonary embolus on the eighteenth postoperative day, which was confirmed by autopsy.

CASE 4.—V. W., No. 353234, a Negro woman, aged 33 years, had been married for four years, but had never been pregnant. Ten days before admission to the hospital she noted lower abdominal pain. Otherwise the history suggested no disease. Physical examination was not important, except for a large mass which filled the pelvic cavity and extended to the umbilicus. Laboratory tests were reported within normal limits. The hemoglobin value was 11.5 Gm. The preoperative sedation consisted of Seconal, grains 3. At operation performed on Feb. 27, 1942 (Hodgkinson), the uterus, including the cervix, right Fallopian tube and ovary, and the appendix were removed. The duration of the operation was 45 minutes. The pathologist reported fibromyomas, chronic cervicitis, chronic salpingitis, and chronic appendicitis. During the first twenty-four hours after the operation she received Pantopon, grain ⅓, for pain. After this period codeine, grain 1, was sufficient for relief of pain. Mild abdominal distention was evident during the first 48 hours postoperatively, but she was taking a full diet without difficulty after 48 hours. The postoperative period was uneventful until her sudden death on the twelfth postoperative day. Skin sutures were removed on the seventh day, at which time the wound was observed to be healing normally. Her temperature was elevated to 100.2° F. on the first postoperative day. The highest recorded temperature for the next seven days was 99.2°. From the eighth postoperative day until the day of her death the temperature was normal. The pulse rate averaged 80 per minute. She was permitted out of bed on the tenth postoperative day. On the twelfth postoperative day she was seized with a severe pain in the chest and died within 30 minutes. An autopsy disclosed a thrombus weighing 16 grams straddling the two main pulmonary vessels. Search for the source of the thrombus was unrevealing.

CASE 5.—N. S., No. 117551, a white woman, aged 65 years, was admitted to the hospital in July, 1948, for treatment of varicose veins. She had worn elastic stockings for years. Numerous incidents suggested that she had had minor thromboses of the superficial leg veins. She also complained of urinary frequency, urgency, and a mass protruding from the vagina. A supracervical hysterectomy had been performed in 1927. Examination disclosed a large cystocele, rectocele, and prolapse of the cervix. Considerable relief was obtained through the insertion of a round, hard, rubber pessary which she wore for the next several months. Vaginal irritation resulted and the pessary was removed. Hypertension 190/110 was present. Preoperative sedation consisted of sodium phenobarbital and scopolamine. On April 12, 1949, (Hodgkinson) the cervical stump was excised and the vaginal wall repaired. The duration of the operation was 75 minutes. Cyclopropane anesthesia was used. Dolophine, 10 mg. every 3 hours, was prescribed for relief of postoperative pain. Her postoperative course was complicated by elevation of temperature to 103.2° F., which was believed to be caused by atelectasis. Under antibiotic therapy the temperature gradually returned to a lower level, but never was normal. She was allowed out of bed on the sixth postoperative day. On the eighth postoperative day a fistulous tract appeared at the upper end of the vaginal canal. Continuous catheter drainage was instituted and the patient was placed on a Bradford frame, face down. April 29, while on a bedpan, she complained of a sudden severe pain in the chest and died within a few minutes. An autopsy disclosed a large embolus in each pulmonary artery. The right common iliac vein was the source of the emboli. A left ureterovaginal fistula accounted for the vaginal drainage of urine. Adhesions from the previous hysterectomy had displaced the ureter to a medial position accounting for the injury. In the care of this patient several important factors contributing to the development of venous thrombosis were overlooked. Extensive varicose veins and the history of repeated minor thromboses in a patient of 65 years of age are ominous signs that should not be ignored. Immobilization on a Bradford frame further increased the hazard of thrombosis. With prophylactic care this tragic incident might have been avoided.

Mention of the mechanics of the circulation suggests that the heart is the motivator. In fact, it is common parlance to refer to the heart as THE pump. Since the arterial phase of the circulation is predominantly accented such a reference is natural. No such positive mechanism exists on the venous side.

The contractions of muscles serve as a subsidiary pump when the venous circulation is considered. As the vein leaves the muscle a valve in the collecting vein distal to the point of exit from the muscle directs the venous flow centrally. The intermittent muscular contractions of the muscles propel the blood onward through the veins.

A third pumping action is provided by respiration. Negative intrathoracic pressure is greater during inspiration than expiration. The downward movement of the diaphragm during inspiration increases the negative intrathoracic pressure, and, at the same time, increases the positive venous pressure below the diaphragm. The negative pressure within the thorax expands the walls of the intrathoracic veins and the venous blood is "sucked" into these veins. The venous blood is, therefore, propelled by the main pump, the heart, and the two subsidiary pumps, muscular and respiratory actions.

The efficiency of respiratory activity as a venous circulatory pump has been demonstrated when the ovarian vein pressure was measured at the operating table.[1] The Trendelenburg position causes the venous pressure in the ovarian vein to fall. Measurement of pressure in the ovarian veins which have no valves can be used to interpret the pressure carried by the systemic venous circulatory system confined within the abdominal cavity. In this instance the ovarian veins act as a side arm manometer. Intra-abdominal venous pressure closely approximates peripheral venous pressure recorded in the veins of the extremities. With a patient in the horizontal position, in the absence of muscular action, the respiratory activity assumes the chief mobilizing influence in transferring venous blood from the abdominal to the chest cavity. In many respects the abdominal veins serve as a reservoir for the temporary storage of venous blood. The respiratory activity of the chest and diaphragm moves the blood to the heart as cardiac action demands. Abdominal distention, abdominal pain, an abdominal incision, and shallow or decreased respiratory activity can easily interfere with the efficiency with which venous blood is mobilized.

Attempts at expiration against a closed glottis produce a positive intrathoracic pressure. The inflow to the heart is reduced. The coronary circulation is inadequate. The systemic venous pressure is tremendously increased and temporary venous stasis occurs.

The effects of gravity are closely allied to the action of the three pumps. In the lower extremities, in the erect posture, the weight of the column of blood tends to increase the venous pressure though this is broken into segments by the valves in the veins. Posture, therefore, has an important bearing on venous flow.

The effect of the vasomotor system on venous flow is well known. The mechanism which controls the vasomotor changes is complex and often obscure. Although definition of the emotions is difficult, the effect of fright and fear on the vasomotor system is readily demonstrated and may play an important role in the circulation of blood. Furthermore, the vasomotor system is greatly influenced by the chemistry of the blood.

Discussion of our fatal emboli has invariably led us to include the fundamental physiologic principles of the circulation of the blood so briefly mentioned. In some instances no apparent cause was found and no warning of the impending danger was given. In retrospect, other fatalities might have been prevented by more careful attention to the preoperative preparation and the circumstances attending the operation.

The report of Case 1 refers to a relatively young (36 years) woman who was apprehensive. She received heavy sedation with morphine both before and after the operation, probably because of her apprehension. Although there was no apparent circulatory impairment before the operation, the heavy sedation

probably produced venous stasis over a period of many hours. The heart rate was slowed, the muscular activity reduced, and the respiratory activity restricted. Chevalier Jackson has long been a crusader against the injudicious use of morphine, atropine, and codeine. He has repeatedly emphasized the harmful effects of these drugs on respiratory physiology because the bronchial secretions are thickened, increasing their adhesiveness and co-adhesiveness. Ciliary action is decreased, the cough reflex is suppressed and the vital capacity is reduced.

The effect of morphine upon the peripheral circulation varies among individuals and also in the same individual. Age of the patient, posture, hemorrhage, and numerous other conditions influence the action of narcotics. Since the precise mechanism of the action of morphine on the peripheral circulation remains controversial, the subject will not be pursued further at this time. There is sufficient evidence, however, to warrant caution in the use of narcotics at the time of operation.

The most apparent error in the management of Case 2 was heavy sedation. When Sodium Amytal was introduced as a sedative, large doses were widely used throughout the country. It was not unusual to see patients arrive at the operating room with slow respiration and pulse. Also, they were totally oblivious to their environment. In addition to the excessive barbital, this patient received morphine after operation. One cannot doubt that the circulation was retarded for a prolonged period. The efficiency of all three physiologic pumps was reduced. The prime requirement for phlebothrombosis was fulfilled.

The emotional reactions of Case 3 were probably not fully appreciated before operation. The management of her fears was not satisfactory. The death of her sister from cancer affected her profoundly and changed her personality. The solicitude of her family, friends, and physician did not allay her cancerphobia. She was aware of a lump in her breast for nine months before consulting a physician and even then avoided a realistic attitude toward her health. The usual assurance was not sufficient to stabilize her emotions. After the operation she was uncooperative, apathetic, and apprehensive. Her apathy prolonged the muscular inactivity long after the effects of the anesthetic. Nurses and physicians caring for her were impressed with her emotional instability. In retrospect, she should have had more intensive psychotherapy.

Careful review of Case 4 revealed no apparent predisposing cause for venous stasis.

The previous history of Case 5 suggested the probability of repeated thrombosis of the superficial veins of the legs. The circulation of a woman 65 years of age with hypertension and previous incidents of thrombosis of superficial veins is compromised. When respiratory embarrassment from atelectasis is added, the risk of venous stasis is sufficient to contraindicate confinement to a prone position.

A great deal has been written about the diagnosis and treatment of thrombosis. The importance of early ambulation has been recognized, but too little attention has been paid to the circumstances before and during an operation. Review of our fatalities has led us to believe that some of them might have been prevented and ''an ounce of prevention is worth a pound of cure.'' A few of the suggestions that have come from our staff discussions may now be mentioned.

The effect of the emotions on the circulation is well recognized. Anxiety, fear, and apprehension have been noted frequently preceding thrombosis. Because of this relation, as well as other physical effects of the emotions, it is desirable to relieve a patient of fear before operation for many reasons. In addition to explanation by the operator to the patient, this duty has been assigned to the residents to comfort the patient the night before operation by answering their questions about the operation. If specific questions are not

asked the resident is expected to mention casually the usual fear of death, of being maimed, of being unsexed, and fear of the anesthetic. Skillful handling of these subjects is more useful in securing a good night's rest than the administration of sedatives. An ideal preparation would be to have the patient eat a good meal, enjoy a pleasant evening, and have a good night's rest such as she would if she had been staying in a hotel.

The dire effect of too much sedation cannot be ignored. If heavy sedation is used the respiration and circulation are depressed and muscular inactivity is prolonged. Add to this deep anesthesia followed by injudicious sedation after operation and the patient has had hours of venous stasis.

The choice of anesthetic is important. One may ask whether spinal anesthesia causes prolonged pooling of venous blood? Does curare promote too much muscular inactivity? Does the operator insist upon deeper anesthesia than necessary? Is the anesthesia stormy with coughing and straining? Regardless of who gives the anesthetic the operator has a responsibility for the welfare of his patient.

The relation of position on the operating table and venous pressure has already been considered, but one feature of the Trendelenburg position deserves special mention. The practice of breaking the table at the knees and strapping the legs to the table not only promotes venous stasis in the veins of the leg, but also could injure the vein. For the same reason a strap during induction of anesthesia could be a source of trouble. The degree of elevation of the table also influences venous pressure.

Laparotomy of necessity alters venous pressure. Abdominal packs may obstruct venous flow. Retractors may unintentionally compress large veins. Thoughtful consideration should be given to the manipulation of viscera.

Thromboembolism remains an urgent problem in spite of extensive investigations. The processes involved are multiple, but circulatory retardation is basic. Vigilance at all times, preoperatively, during operation, and postoperatively, should reduce the incidence of embolism. Attention is invited to the possibility of prevention by an appreciation of the physiologic principles of venous circulation and by endeavoring to keep that circulation within physiologic bounds at all times. Emphasis has been focused upon the preoperative period as the time to begin prevention.

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Discussion

DR. LOUIS E. PHANEUF, Boston, Mass.—Dr. Pratt and his co-workers have brought to our attention an important and serious complication of gynecological surgery. They review and condense the mechanics of the circulation as they influence the precursors of embolism, namely, phlebothrombosis and thrombophlebitis. They intentionally omit injury to the veins and blood chemistry, which are important to the process of thrombosis, in order to focus attention on the role that is played by venous stasis.

The statistics of the Gynecological Department of the Henry Ford Hospital, since the opening of the Department in 1926, show an incidence of 23 fatal emboli in 17,742 patients upon whom operations were performed during a period of 24 years. Pertinent data of 5 cases of fatal embolism are presented in the form of case reports. I have had the statistics of the Gynecological Department of the Carney Hospital reviewed for a period of ten years, from January, 1941, to January, 1951. During this period of ten years 6,530 gynecological patients were admitted. There was one fatal case of pulmonary embolism in the group.

Case Report.—A 47-year-old, married, white woman was referred to the hospital by her family physician because of a fibromyoma which rose to the level of the umbilicus. On April 26, 1945, she had a panhysterectomy, bilateral salpingo-oophorectomy, and appendectomy

performed. The convalescence was simple, her temperature rose to 101° F. on the second postoperative day, thereafter it remained normal. The skin sutures were removed from a healed incision on the eighth day. At no time during the convalescence did she have any signs of thrombosis, there was no swelling of the lower extremities; the Homans' sign was absent. On the morning of the fourteenth postoperative day she was examined by me. The incision was well healed, there was no abdominal tenderness, the vaginal vault was healed and well supported and there were no masses or areas of tenderness in the pelvis. The lower extremities showed no evidence of circulatory disturbance. She was discharged and left the hospital the same forenoon. Upon her arrival home she developed cyanosis, tachycardia, and dyspnea. Her family physician was called, he gave her some oxygen, and sent her back to the hospital in an ambulance, where she arrived moribund, and died from pulmonary embolism twenty minutes after admission. A necropsy was refused.

From 1944 to 1951 ten prophylactic superficial femoral vein ligations were performed preoperatively. The youngest patient was 39 and the oldest 64 years of age. Four ligations preceded abdominal panhysterectomy and six preceded vaginal plastic surgery. There was no occurrence of emboli in these patients.

In attempting to combat thrombosis and embolism we have as prophylactic and therapeutic agents: (1) early ambulation; (2) prophylactic vein ligation, and (3) the anticoagulants, heparin and Dicumarol. The essayists further advise that prophylaxis begins before operation, extends during operation, and terminates only after the postoperative period. They offer the following suggestions: (1) relieving the patient of fear before operation, allaying the fear of death, of being maimed, of being unsexed, and the fear of the anesthetic— this is best carried out the evening before operation; (2) the avoidance of too heavy sedation; (3) the choice of anesthesia, avoiding deeper anesthesia than necessary; (4) the position on the operating table, Trendelenburg position, binding the legs, etc., bearing in mind that abdominal packs, retractors, and manipulation of viscera all alter venous pressure.

With these suggestions in mind and with constant vigilance we should be able to reduce still further the incidence of thromboembolism.

DR. CONRAD COLLINS, New Orleans, La.—Dr. Pratt has presented a timely subject. We have not been as fortunate in New Orleans as he has been in Detroit, as we think that we have a relatively high incidence of thrombosis and embolism in the Charity Hospital. We wish to emphasize that we do not use anticoagulants or venous ligation prophylactically. We use therapy only when signs of thrombosis develop. And our therapy is surgical. Therapy on our service consists of bilateral superficial femoral ligation in cases where phlebothrombosis in the leg veins is suspected. Should the clot extend higher into the common femoral, then we seriously consider and do ligation of the vena cava. We have had two patients who subsequently died of thrombosis, in whom the thrombus extended higher in the common femoral and was removed by suction and the superficial femoral veins tied. Evidently the thrombus re-formed higher than the point of ligation and fatal pulmonary embolism developed. Since that time, when the clot extends higher than the junction of the superficial and deep femoral veins and if it extends into the common femoral veins to a point higher than we can ligate, the vena cava is ligated by an extraperitoneal approach or, after the clot has been removed by suction, the patient is treated with anticoagulants, both of these methods being an added precaution against subsequent development of the clot and embolism. For suppurative pelvic thrombosis that fails to respond to medical regimen, we ligate the normal venous return from the uterus, that is the vena cava and both sets of ovarian vessels. There are many prophylactic means that we should employ in our efforts to reduce the incidence of intravascular clotting. Every patient whose history is taken should be asked whether or not there was any history of previous thrombosis. If so this patient should be more carefully watched postoperatively and postpartally than others, as persons who are once clotformers usually repeat. At the first sign of any clotting, therapeutic measures should be instituted. Other methods of prophylaxis, of course, are vigorous movement of the legs in bed and early ambulation. Any position or use of any apparatus which produces pressure in the popliteal space should be avoided. This is especially true of the newer leg holders, which are used

during delivery or vaginal plastic work or vaginal hysterectomy. It is also true of some of the leg holders which are part of apparati designed to supply heat to the perineum. In a twelve-year study of thrombosis and embolism at Charity Hospital, covering the period 1938-1950, just completed by Drs. DeCamp, DeBakey, and Ochsner, it was found that there has been an increase in thrombosis and embolism on the wards of Medicine, Surgery, and Neurology, and a decrease in the last few years in the Department of Gynecology and Obstetrics. We believe the decrease has been due to the prophylactic measures that we have used. And again we wish to reiterate that we have not used anticoagulants, anti-thrombants, or surgery prophylactically. Thrombosis and embolism are one of the major causes of fatality in gynecologic surgery today. The treatment of thrombosis begins with its prevention, constant efforts to detect the signs and symptoms of early thrombosis, and the institution of therapy when the signs or symptoms develop, be that therapy surgery, anti-coagulants, or both.

DR. PRATT (Closing).—I wish to thank the discussants. Dr. Phaneuf was requested to discuss this subject as his meticulous care of his patient exemplifies many of the features suggested.

NUTRITIONAL DEFICIENCIES AS A CAUSAL FACTOR IN TOXEMIA AND PREMATURE LABOR*

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PRESENT-DAY views on the etiology of the various dysfunctions of pregnancy, which have in any way considered the role of nutrition as a causative factor, have been concerned only with diet as a primary factor of consideration. In other words, faulty diet has been viewed as the sole contributory cause. This error of thinking has resulted logically, since all efforts at the detection of variants in physiology and metabolism have been directed toward specific nutrient elements, and it was supposed that each essential nutrient produced a specific disturbance completely unrelated to other elements or their functions. Consequently, diet has been stated to be in no way related to the occurrence of dysfunction in those patients who were considered to have had an adequate diet, and yet in whom complications have developed. Further, these observers have restricted their point of view to a theoretical or arbitrary evaluation of adequacy in the diet, and have ignored those other factors, which, in many instances, have a greater effect on nutrition than actual food intake. They have completely ignored the fact that a diet as such may be completely adequate yet the patient develop a nutritional deficiency state. This still remains, after these many years, a most difficult point of understanding for these observers, since they continue to interpret nutrition as purely concerned with dietary intake, omitting entirely consideration of the nutritional requirements of the patient and the factors which can materially, and often drastically, alter her requirements or the nutrient supply necessary for the support of pregnancy.

In recent years it has become evident that these problems are not separate clinical entities which can be expected to respond to some simple specific therapeutic agent. On the contrary, they result from complex, closely interrelated dysfunctions of the individual patient's metabolism and physiology; or, in brief, alterations in nutrition.

Metabolism is concerned with the development, maintenance, destruction, and chemical changes occurring in the cell by which energy is provided for the vital processes and activities characteristic of a specific cell. New essential nutrients are necessary for this process. This process may be regarded as including two aspects: first, anabolism (constructive), which in general is a synthetic process resulting in the utilization of essential nutrient substances for the pur-

pose of creating the more complex end result which constitutes the living cell; second, catabolism (destructive), in which the constituents of the cell are reduced to simpler elements with the liberation of energy. These two processes occur simultaneously and one may predominate and obscure the other. The adequacy and availability of essential nutrients determine which process becomes dominant. In brief, therefore, if the quantity and quality of the essential nutrients reaching the cell are optimum, anabolism will predominate and the cell remains in a state of positive nutritional balance.

Physiology is concerned with the function or activity for which the cell is specifically designed. The efficiency with which a cell functions is determined by the efficiency of the metabolic process within the cell; it is a process entirely apart from metabolism although intimately and directly dependent upon it.

Nutrition, therefore, is the sum of the processes by which an organism absorbs and utilizes essential nutrients for the support of metabolism within the cell, stores for future use, or uses immediately for energy. It is, further, the process by which the organism absorbs, transports, utilizes, and stores essential nutrients and other substances in the metabolic process of the cell and in addition thereby makes possible the specific function of a cell; but it also includes the sum of the influences which the intrinsic and extrinsic environment exert upon these processes.

Diet aids in the support of nutrition, but is *not* nutrition, and in pregnancy usually becomes secondary in importance to the many other conditions which can influence individual nutrition. It is, therefore, essential to the adequate understanding of the newer concept of the roles of nutrition and nutritional deficiencies in pregnancy, that the proper relationship between the various conditioning factors and diet be understood.

Weight in Pregnancy

Among the many changes occurring in pregnancy, the result of alterations in metabolism or physiology, one of the most significant is the change in the patient's weight. The allowances for weight changes in pregnancy, as reported in the literature, vary over such a wide range as to become fantastic. These allowances have been based in most instances on bizarre or "fetish" approaches to the problems of the patient's needs. Unfortunately, there has been little factual consideration of the actual physiological changes and metabolic needs, which predicate the alterations in weight which should be expected.

An analysis of our data for gains in weight of selected patients resulted in a total average cumulative gain in weight during pregnancy of 24.0 pounds. The cumulative curve by weeks of gestation is shown in Fig. 1.

Since this curve has been used as a base line for evaluation of significance of variations in gain in weight by individual patients in several analyses presented in this report, the methods used in obtaining it are described in detail. An average curve for gain during the entire prenatal period was desired that, at least, could be considered representative of the gain experienced by those patients who had had the most satisfactory pregnancies. Although the ideal, or optimal, gain is not necessarily represented by average gain for patients without complications and without major signs or symptoms of dysfunction, the average curve for such patients does describe gain in weight that is compatible with a better-than-average pregnancy from a clinical point of view.

The curve for gain in weight was developed in two stages: first, the *observed* cumulative change during the second and third trimesters; and second, the reported change from pregravid weight to the end of the first trimester, which, when added to the curve from the last two trimesters, gives the total net gain during pregnancy.

The average curve for weight gained in the second and third trimesters is based on data for 60 patients carefully selected from about 600. Their reported weights at the beginning of pregnancy were within 10 per cent of the standard weight for height. All had been delivered of a full-term living infant. None had had any definite prenatal complications; during their prenatal course 2+ or persistent edema did not occur (some had slight edema noted once or twice), the diastolic blood pressure did not exceed 88 and 2+ nausea or vomiting did not occur at any time. All made their first visits to the clinic not later than the thirteenth week of gestation and the first recorded weight was equal to or greater than the reported pregravid weight with the exception of that of two patients whose weight loss was less than 2 pounds.

For the 60 selected patients, the average weekly gain in weight from 13 weeks to 39 weeks of gestation was computed. The weekly gain or loss for each patient was obtained by dividing weight change for the interval between two visits by the number of weeks, usually 3 weeks until about the last six weeks of pregnancy when bi-weekly visits were made by the majority. The average weekly gains were cumulated and the final curve was smoothed.

It would appear that those who advocate a total gain in weight during pregnancy of 12 to 15 pounds will of necessity have to meet the necessary metabolic and physiologic requirements at the expense of the maternal host. It should be further obvious that this can result only through the creation, or further exaggeration, of a deficiency state and a concomitant catabolic process. In order to accomplish such a drastic restriction in a normal weight patient's gain in weight, there would have to be dangerous limitations established in regard to essential nutrients as well as actual caloric intake. These caloric restrictions would obviously have to be well below basal requirements, let alone those needed for the maintenance of energy requirements during pregnancy, and for fetal growth. There can be no rationale in any procedure which is predicated on such a process.
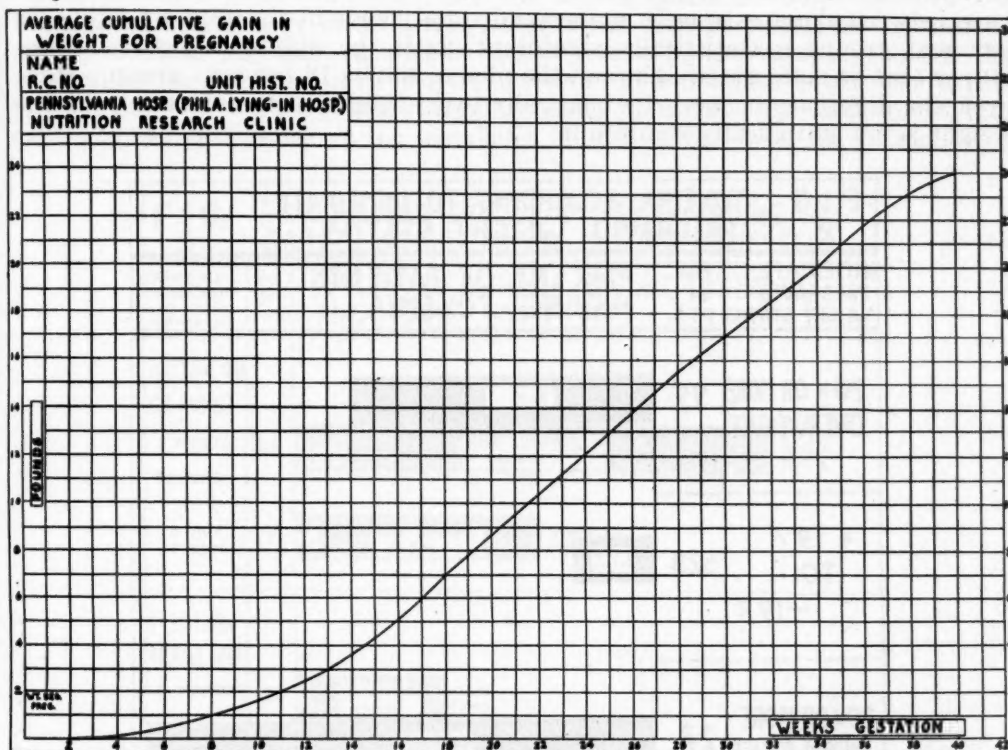
Toxemias of Pregnancy

It is generally considered that the term "toxemia of pregnancy" is a misnomer. It appears to us that alterations in metabolism and physiology, which constitute the nutritional process within the individual, will directly affect the physiology and metabolism within the pregnancy itself. Therefore, it is our opinion that the so-called "toxemias of pregnancy" are in reality nutritional deficiency states. If this be true, there must be a demonstrable relationship between the nutrient needs during the nonpregnant state and the increased needs occurring as the result of pregnancy.

Various criteria from which evidence can be obtained to indicate individual status are available from chemistry including hematology, certain objective data such as the patient's weight, blood pressure, the absence or presence of edema, and response to dietary supplements. No single finding is pathognomonic of toxemia and several findings are associated usually in the early stages as well as the later stages of actual breakdown. Some are more directly critical than others, and some will precede others in their observable occurrence. Thus the problem becomes one of interpretations made against known base lines of acceptability, in formulating judgment at any specified time in pregnancy as to the possible development of deviations which are not compatible with a satisfactory prenatal course.

Fortunately, there is a very close relationship between the causes which produce these deviations and observable alterations which occur. Ample warning is available that dysfunctions are developing prior to their becoming clinical catastrophes. Unfortunately, most of the considerations given to the catastrophes have been concerned with these catastrophes after they have occurred.

FIG
1

Among the clinical findings of major importance in evaluating an individual's status at any time during pregnancy is her weight—weight at the beginning of pregnancy in relation to her standard weight and the rate of gain in weight during the three trimesters in relation to the normal rate of gain. It has long been recognized that the individual definitely overweight at the beginning or who gained excessively during pregnancy has an increased incidence of preeclampsia and eclampsia. However, the literature is essentially devoid of consideration given to those individuals who are markedly underweight; yet these individuals account for nearly twice the incidence of toxemia compared to those overweight. It should have been obvious that the underweight individual has a markedly increased hazard when confronted with any increased stress factor in that she not only has failed to obtain the essential nutrients necessary for the maintenance of adequate physiology and metabolism; but also has failed to obtain even a gross caloric intake sufficient to maintain body weight in relation to energy requirements. The overweight individual has a gross caloric intake in excess of her energy requirements and consequently a greater chance of obtaining some of the essential nutrients necessary for maintenance. It is known that individuals of standard weight, like those above standard weight, can be deficient as the underweight individual always is; but the individual who is

standard weight or above has the better chance of fulfilling nutrient needs than the underweight individual under comparable stress conditions.

There are two categories of immediate pregravid weight that significantly increase the probability of toxemia. Fig. 2 fully illustrates the significance of the three weight classifications. This table considers only the weight of the patients at the time they became pregnant, and the incidence of toxemia in relation to this weight, and does not consider what they did during the interval between the beginning of pregnancy and the onset of the toxemia. The difference between those extremely underweight and those in the plus or minus 19 per cent groups is statistically significant, as is the difference between those 20 per cent or more overweight and the plus or minus 19 per cent group. However, the difference between the markedly overweight and the extremely underweight is not statistically significant.

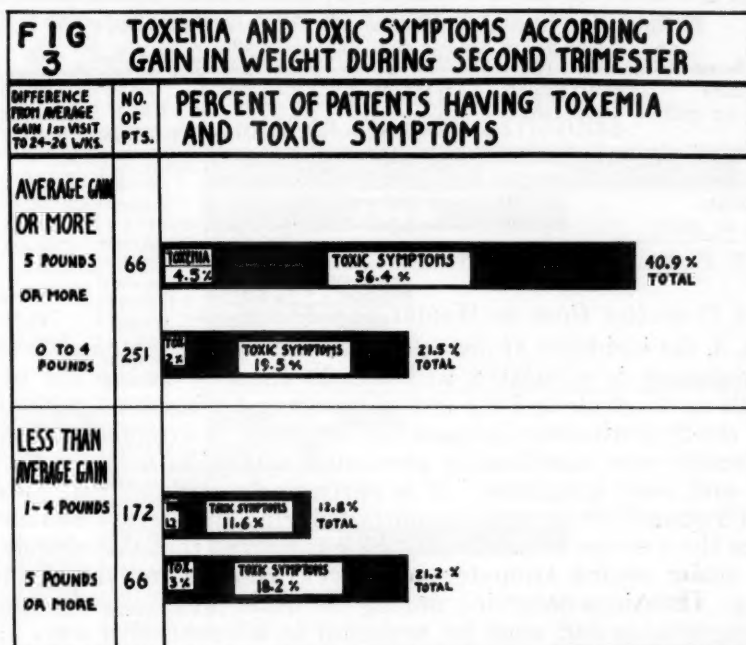| FIG 2	TOXEMIA ACCORDING TO IMMEDIATE PREGRAVID WEIGHT STATUS	
IMMEDIATE PREGRAVID WEIGHT STATUS	NO. OF PTS.	PERCENT OF PATIENTS HAVING TOXEMIA
20% OR MORE OVERWEIGHT	99	6%
+19% TO -19%	528	1.7%
20% OR MORE UNDERWEIGHT	27	11.1%

Prenatal Weight Changes and Toxemia.—

Excessive gain in weight is well known as a concomitant to toxemia if not conducive to its development. The clinician is interested in how much or how little gain in weight is compatible with a favorable course of pregnancy, and at what level should a variation in gain in weight be considered a sign of potential or developing toxemia.

Analysis of the relation of gain in weight to the incidence of toxic symptoms is complicated by the fact that weight, especially increase in weight, is not independent of the toxic condition itself, since edema (fluid retention) almost always accompanies toxemia and contributes to the observed weight increase. The scale measures only the added pounds and does not differentiate the nature of the gain. Considerable fluid retention may be present before edema becomes an objective finding, thus the exact time dysfunction commences cannot be identified. Therefore gain in weight previous to the onset of fluid retention cannot be determined accurately, either for patients who eventually develop an objective toxic syndrome or for those who do not, but who may

have temporary nutritional failure without definite objective signs of toxemia. The incidence of toxic symptoms according to weight changes prior to their onset is needed to obtain evidence as to the amount of gain in weight that gives adequate support to the needs of pregnancy and does not add to the stress of pregnancy.

In the following analysis of gain in weight during the three trimesters of pregnancy in relation to the incidence of toxic symptoms or toxemia, only the extent to which these symptoms occurred among patients with a specified net increase in weight over an arbitrary interval of time is indicated. A patient may shift from one gain in weight category to a higher category within the interval as the result of a developing toxemia, and the case is charged to the incidence for the higher gain in weight category although a previous inadequate gain was the true cause of the metabolic failure. Therefore, the incidence of

FIG 3 — TOXEMIA AND TOXIC SYMPTOMS ACCORDING TO GAIN IN WEIGHT DURING SECOND TRIMESTER

toxic symptoms among patients with a given gain in weight over a three months' period cannot be considered reliable evidence of the importance of this gain, as a predisposing factor to the occurrence of toxemia, unless the presence or absence of edema is also evaluated. The relative incidence rates according to various amounts of gain at the end of specific trimesters does afford information on the probability that toxemia may develop.

First Trimester Gain in Weight and Toxemia.—

In the discussion of premature labor, it is emphasized that initial weight and behavior during the first trimester are both important. However, the incidence of toxemia and other toxic symptoms did not differ significantly when related to weight changes during the first trimester. It is very evident in Table I, however, that there is a definite tendency for the incidence of toxemia and/or toxic symptoms to increase as the rate of gain in weight increases during the first trimester. This must be considered an early warning even though these weight changes are not as significant in relation to the development of toxemia or toxic symptoms as changes occurring later in pregnancy. This is understand-

able, assuming that the requirements of pregnancy are adequately met during
the last two trimesters, in that the individual can begin pregnancy with a suf-
ficient nutrient reserve to meet the demands of the first trimester. Weight
behavior during the first trimester does not necessarily indicate a patient's ability
to adjust to the stress of later pregnancy, and may only indicate an unsatisfactory
pregravid nutritional status which must be corrected.

TABLE I. FREQUENCY OF PRE-ECLAMPSIA AND TOXIC SYMPTOMS ACCORDING TO WEIGHT GAIN
OR LOSS DURING FIRST TRIMESTER*

CHANGE FROM PREGRAVID WEIGHT TO 12-16 WEEKS	NO. OF PATIENTS	PRE-ECLAMPSIA	ELEVATED DIASTOLIC PRESSURE WITH EDEMA AND ADM. FOR STABILIZATION	EDEMA 2+ OR PERSISTENT	TOTAL PRE-ECLAMPSIA OR SYMP-TOMS
		Number of Patients With Symptoms			
All patients	555	12	50	55	117
Gain 6 pounds or more	148	2	19	18	39
Gain 1-5 pounds	246	7	19	25	51
Weight loss, no gain	161	3	12	12	27
		Percentage of Patients With Symptoms			
All patients	100.0	2.2	9.0	9.9	21.1
Gain 6 pounds or more	100.0	1.4	12.8	12.2	26.4
Gain 1-5 pounds	100.0	2.8	7.7	10.2	20.7
Weight loss, no gain	100.0	1.9	7.5	7.5	16.8

*Patients 20 per cent or more overweight not included.

Second Trimester Gain in Weight and Toxemia.—

In Fig. 3, the incidence of pre-eclampsia and toxic symptoms which occurred
later in pregnancy is correlated with weight changes during the period from
the first visit to the clinic and the end of the second trimester. Although weight
changes in the first trimester increase the incidence of symptoms, changes in the
second trimester were significantly associated with differences in the incidence
of toxemia and toxic symptoms. It is particularly striking that those patients
who gained 5 pounds or more above normal during this period had an incidence
nearly twice the average rate. It must be emphasized that this change in weight
is for the entire second trimester, or longer, not for individual intervals of
visits. Thus, variations occurring during the usual prenatal visit intervals take
on added importance and must be projected in a cumulative way, to a period
later in pregnancy, if the true significance of the change is to be apparent.

In other words, during most of the second trimester the weekly weight
change is 0.8 pound per week. Consequently, during this three months' period,
patients who add, for example, 5.5 pounds per month, are too frequently dismissed
with little consideration being given to such a gain, whereas if this rate of gain
in weight continues throughout the second trimester, it will amount to slightly
over 6 pounds excess gain for this period. Fig. 3 shows that this gain which is
generally considered to be only slightly excessive doubles her chances of be-
coming pre-eclamptic over those of the individual whose rate of gain is normal
and this applies equally to the incidence of toxic symptoms.

Third Trimester Gain in Weight and Toxemia.—

The true significance of variations from an acceptable rate of gain during
the first two trimesters becomes more apparent as the changes in rate of gain
during the third trimester are correlated with the pattern of gain in weight
during the previous two trimesters. In Fig. 4, the gain in weight during the
third trimester is considered in relation to the gain in weight previously observed.
Although the number of cases in some weight-change subdivisions becomes too

few to provide reliable percentages for comparison statistically, the variations in the occurrence of toxic symptoms suggest that some inferences can be drawn concerning the association between gain in weight and the incidence of toxic symptoms.

First, in patients who gained excessively up to the end of the second trimester, and continued to gain at more than the average rate in the third trimester, the incidence of toxic symptoms was about 50 per cent. Furthermore, approximately two-thirds of the patients who had gained excessively by the end of the second trimester did continue to gain at the average rate or higher in the third trimester. For those few patients whose gain in the third trimester was greatly reduced, the incidence of toxic symptoms was noticeably reduced. Presumably, these were brought under control, fluid loss occurred and metabolic balance re-established.

FIG 4 — TOXEMIA OR TOXIC SYMPTOMS ACCORDING TO GAIN IN WEIGHT DURING SECOND AND DURING THIRD TRIMESTER

GAIN SECOND TRIMESTER	GAIN THIRD TRIMESTER	PERCENT OF PATIENTS DEVELOPING TOXEMIA OR TOXIC SYMPTOMS
5 POUNDS OR MORE ABOVE AVERAGE	ABOVE AVERAGE 4 POUNDS +	61.5 %
	AVERAGE ± 3 POUNDS	41.9 %
	BELOW AVERAGE 4 POUNDS +	10 %
0-4 POUNDS ABOVE AVERAGE	ABOVE AVERAGE 4 POUNDS +	23.4 %
	AVERAGE ± 3 POUNDS	20.9 %
	BELOW AVERAGE 4 POUNDS +	22 %
BELOW AVERAGE 1-4 POUNDS	ABOVE AVERAGE 4 POUNDS +	22.2 %
	AVERAGE ± 3 POUNDS	12.9 %
	BELOW AVERAGE 4 POUNDS +	5.9 %
BELOW AVERAGE 5 POUNDS OR MORE	ABOVE AVERAGE 4 POUNDS +	41.7 %
	AVERAGE ± 3 POUNDS	21.2 %
	BELOW AVERAGE 4 POUNDS +	11.1 %

Second, the incidence of patients with toxic symptoms was high—41.7 per cent—among the small number of patients who had gained 5 pounds or more less than average by the end of the second trimester, and then gained 4 pounds or more in excess of average during the third trimester, which represents a very marked shift in the rate of gain. To a lesser degree, an increase in the incidence of toxic symptoms occurred among patients who had gained 1 to 4 pounds less than average in the second trimester and who gained in excess of 4 pounds or more in the third trimester.

Third, for each group of patients classified according to the second trimester weight gain, the incidence of patients with toxic symptoms is about the same for those whose gain in the third trimester was not more than 3 pounds above average gain in weight, and those whose gain in weight was not more than 3 pounds below average. However, the incidence of toxic symptoms varies according to the gain in weight during the second trimester, and this suggests that the probability of developing toxemia is, in the majority of patients, determined by the gain in weight which is established by the end of the second trimester.

Thus it becomes apparent that previous attitudes which disregarded the patient's nutrient needs during the first two trimesters, together with her rate of gain during this period, allowed a metabolic and physiologic pattern to become established which seriously increases the probability of the development of toxemia. This becomes particularly critical among those individuals whose nutrient reserves are in deficit at the time they become pregnant, or whose nutritional status is further depleted by uncorrected nausea and vomiting or any other conditioning factors which increase the relative stress to which the individual is subjected during pregnancy. It further emphasizes the desirability of maintaining an approximately normal rate of gain during the first two trimesters to preclude the hazards of pre-eclampsia by avoiding an excess rate of gain. It must also be noted that an excessive restriction in the rate of gain during this period seriously increases the incidence of premature labor. Also, a failure to gain at a normal rate during the first two trimesters must not be compensated for, beginning during the latter part of the second trimester, in an attempt to avoid premature labor. Such a procedure may then move the patient directly into the zone of toxemia and the incidence of severe pre-eclampsia and eclampsia increases almost proportionately to the rate of gain in weight especially during this period.

FIG 5 TOXEMIA AND SUPPLEMENTATION

RESEARCH CLINIC GROUP	NO. OF PTS.	PERCENT OF PATIENTS HAVING TOXEMIA
CONTROL	170	4.12%
VITAMIN THERAPY	244	3.28%
PROTEIN THERAPY	186	2.69%
VITAMIN+ PROTEIN THERAPY	160	0.63%

When patients have gained excessively, or show a tendency toward increasing gain, a lessening in the rate of gain during the third trimester sets up a protective mechanism against toxemia. However, this reduction in the rate of gain can also terminate in disaster if the reduction in gain is not accompanied by a continuation of an intake of essential nutrients with a reduction in total caloric intake, rather than an indiscriminative quantitative reduction. There are, however, those individuals who must of necessity maintain their physical activity at peak levels, and they must be protected by adequate nutrient intake sufficient for their continued needs, together with sufficient caloric intake to preclude any possible tissue catabolism to meet these needs.

Toxemia, Toxic Symptoms and Supplementation.—

Among 760 single* viable births there were 21 cases of toxemia. The toxemia rate for those in the control group and in the different nutrition-supplemented groups is shown in Fig. 5.

It is apparent that although the vitamin and protein supplemented groups had a slightly lower percentage of patients with pre-eclampsia, these groups do not differ significantly from the control group. But among women who received both vitamins and protein, there was only one case of pre-eclampsia, 0.63 per cent, or about one-sixth of the rate among patients in the control group. The difference is significant according to conventional standards, since, on the basis of the numbers of patients in the groups, the chances are slightly less than 5 in 100 that this difference or a larger difference would occur from chance alone.

Although the incidence of diagnosed pre-eclampsia was lower in the supplemented groups than in the control group, there was very little difference in the incidence of patients with toxic symptoms as shown in Table II. Thus, the difference has been chiefly in the frequency with which the toxic patient advanced to the pre-eclamptic state. This difference is most apparent between the control group and those who received both vitamins and protein; in the control group 18 per cent of the patients with toxic symptoms became pre-eclamptic; but when both supplements were taken only 3 per cent of the patients with toxic symptoms became pre-eclamptic.

TABLE II. INCIDENCE OF PATIENTS WITH PRE-ECLAMPSIA BY STUDY GROUPS

| STUDY GROUP | NUMBER OF PATIENTS | PATIENTS WITH TOXIC SYMPTOMS | | | |
| | | PRE-ECLAMPSIA EXCLUDED | | PRE-ECLAMPSIA INCLUDED | |
		NO.	%	NO.	%
Total	760	160	21.2	181	23.8
Control group	170	39	22.9	46	27.1
Vitamins only	244	48	19.7	56	23.0
Protein only	186	39	21.0	44	23.7
Vitamins and protein	160	34	21.3	35	21.9

Premature Labor

The problem of "prematurity" is generally considered to be a pediatric rather than an obstetric problem; but obviously, without premature labor, there would not be a premature baby. Consequently, a new approach must be undertaken, directed toward some preventive or remedial procedures which would eliminate the possibility of, or the causative factors concerned with, the early onset of spontaneous premature labor. Eastman,[1] in his most recent textbook, demonstrates that approximately seventy per cent of premature labors were of spontaneous onset, in single pregnancies and without known cause.

Data obtained from our preliminary clinical investigation[2] demonstrated the definite association between adequate nutrition in the mother and premature labor. It was demonstrated that the research group had an incidence of premature labor 41 per cent lower than that of the control group. This strongly suggests that the improvement in maternal nutrition affected a marked lowering in the incidence of premature labor among those patients for whom Eastman

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*Excluded are eight twin births among research clinic patients, 5 were premature and 3 at term. One case of pre-eclampsia occurred in a mother who had a term twin birth; she had been receiving a protein supplement. In addition, 8 women have been excluded from the study because of chronic heart or kidney diseases or essential hypertension. There were two cases of pre-eclampsia among these 8 patients. One of the patients having essential hypertension who became pre-eclamptic was in the control group; the other was in the group which received protein supplementation only.

finds no specific cause available. This 41 per cent reduction in premature labor would account for more than half of the 70 per cent of single pregnancies in Eastman's series which terminated prematurely and without known cause.

Throughout the present study an individual patient's weight at any specific time in pregnancy, and her immediate pregravid weight, have taken on increasing significance. It has become apparent that patients beginning pregnancy obviously underweight or overweight have an increased incidence of catastrophes; and those commencing pregnancy at standard weight, but whose pattern of gain fails to follow the standard pattern, also have an increased incidence of catastrophe. In analysis of the data available of those patients who had catastrophes or whose babies were unsatisfactory, two very striking patterns developed. The first was characterized by increased maternal catastrophes occurring among patients whose gain in weight pattern was definitely in excess of average; the second pattern, and equally characteristic, produced an increased incidence of infant catastrophes, and was conspicuous among those patients whose weight was markedly below standard at the beginning of pregnancy or who failed to gain satisfactorily during pregnancy.

Data relative to the patient's weight at the time she becomes pregnant, and her gain in weight during pregnancy, have produced a pattern as indicative of the increased probability of premature labor as was found relative to toxemia. This pattern differs completely, however, from that associated with toxemia except that the individual who is underweight at the time she becomes pregnant is the greatest obstetrical hazard, having the greatest probability of both toxemia and premature labor.
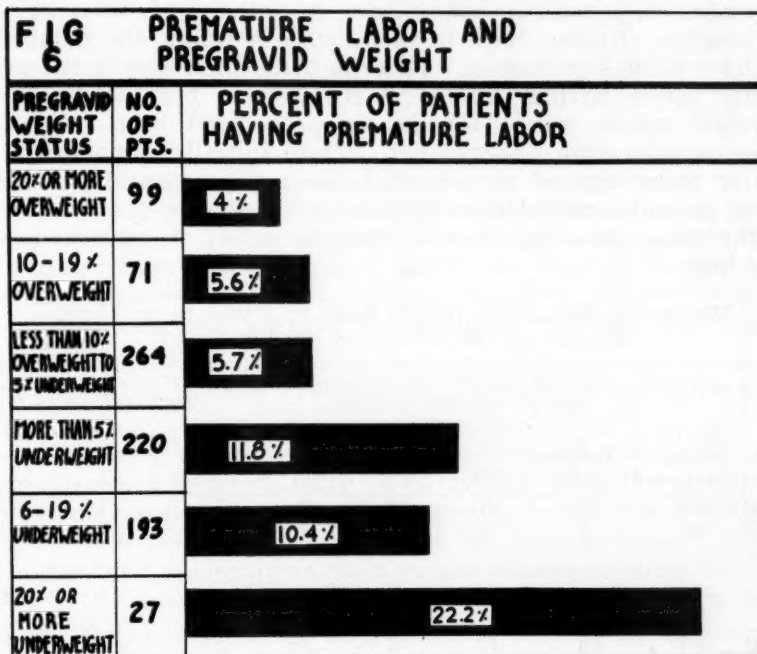
If remedial procedures are to be instituted in an effort to preclude the onset of premature labor, every effort must be made as early in pregnancy as is possible; since the pattern for spontaneous premature labor is established very early in pregnancy, and by the end of the second trimester this pattern cannot be altered.

In Fig. 6, the frequency of premature labor according to immediate pregravid weight status of the patient amply demonstrates that among patients of standard weight or above the incidence of premature labor was essentially the same. Among the patients 5 per cent or more underweight, the incidence of premature labor is twice as high as among those of standard weight or above; and is almost four times as high among those patients 20 per cent or more underweight. The causal relationship suggested by this striking difference in the rate of premature labor has apparently been overlooked in practically all considerations of this problem. It should have become obvious long ago that the individual markedly underweight is not obtaining a sufficient quantity of nutrient intake to maintain standard body weight, and is certainly lacking in the essential nutrients necessary for the support of normal body function. It is also rational to assume that since adequate nutrition is necessary for the maintenance of normal body function, successful support of pregnancy will require an added intake of essential nutrients.

For many years we have recognized that the so-called toxemias of pregnancy were in reality nutritional deficiency states, and that prognostication as to the onset of pre-eclampsia could be established well in advance of the development of this clinical syndrome; but there has been a conspicuous lack of observed patterns indicative of an increased probability of onset of premature labor. Consequently, a pattern which indicates early in pregnancy the probability of premature labor, based on any consistently appearing set of conditions, significantly contributes to the clinical management of this problem which accounts for the highest single cause of infant loss.

It must be emphasized that a substandard weight greater than 5 per cent increases the probability of premature labor over that in patients who are

standard weight or above. This difference is statistically significant. Fig. 6 further indicates that the patient 20 per cent or more overweight (the obese woman) also had a lower rate than the underweight patient and has a certain amount of protection against premature labor. This is understandable since the individual of standard weight or above, even including those who are definitely obese, has a greater probability of obtaining essential nutrients necessary to support pregnancy successfully to a point beyond which the infant would be classified as premature. It should be noted that among the 654 patients analyzed in Fig. 6, the over-all rate for premature labor was only 7.5 per cent and is lower than rates usually reported. This rate of 7.5 per cent, even including those having an excessively high rate, indicates rather dramatically that from the standpoint of premature labor nutrition must play a very dominant role even though the nutritional status of individual patients may not always be optimum.

FIG 6. PREMATURE LABOR AND PREGRAVID WEIGHT

PREGRAVID WEIGHT STATUS	NO. OF PTS.	PERCENT OF PATIENTS HAVING PREMATURE LABOR
20% OR MORE OVERWEIGHT	99	4%
10-19% OVERWEIGHT	71	5.6%
LESS THAN 10% OVERWEIGHT TO 5% UNDERWEIGHT	264	5.7%
MORE THAN 5% UNDERWEIGHT	220	11.8%
6-19% UNDERWEIGHT	193	10.4%
20% OR MORE UNDERWEIGHT	27	22.2%

Since the premature labor rate is higher among Negro than among white patients, Table III is included to establish the fact that a similar association between pregravid weight and the incidence of premature labor is found for both white and Negro. It will be noted that again it is the individuals who are 5 per cent or more underweight who have the higher rate of premature labor and that those who were standard weight or above were protected.

It is interesting to note that the Negro patient 5 per cent or more underweight also had a rate which is almost twice as high as for those standard weight and above; but there is little difference among the standard weight and overweight patients as appears among comparable white patients. This difference in the incidence of premature labor among the Negro patients probably results from more severe and prolonged depletion of their nutrient reserve. It may further indicate that they were less able to accomplish a protective level sufficiently early in pregnancy. They are seen at the same time prenatally as are the white patients and receive the same prenatal care, which strongly suggests that the difference between these two groups must lie in the nutrient reserve status available at the time they become pregnant.

TABLE III. FREQUENCY OF PREMATURE LABOR FOR WHITE AND NEGRO PATIENTS CLASSIFIED BY IMMEDIATE PREGRAVID WEIGHT STATUS

	WHITE			NEGRO		
WEIGHT STATUS	NO. OF BIRTHS	PREMATURE		NO. OF BIRTHS	PREMATURE	
		NO.	%		NO.	%
Total	509	26	5.1	145	23	15.9
10 per cent + overweight	123	2	1.6	47	6	12.8
Less than 10 per cent Over to 5 per cent underweight	214	9	4.2	50	6	12.0
More than 5 per cent underweight	172	15	8.7	48	11	22.9

Table IV is interesting to examine since it is broken down by differences in weight status of premature babies born to patients of different immediate pregravid weights. Broken down in such detail, however, the numbers become too few to have much significance. There is little difference in the proportions of premature babies having different birth weights born to the mothers of different weight status, except for the six prematures born to mothers who were 20 per cent or more underweight. These initially underweight patients had a greater percentage of very small babies. This suggests that the better an individual patient's metabolic and physiologic reserve at the time she becomes pregnant, the more probably she will continue safely to term and produce a satisfactory baby.

TABLE IV. WEIGHT OF PREMATURE BABIES BORN TO PATIENTS OF DIFFERENT WEIGHT STATUS AT THE BEGINNING OF PREGNANCY

PATIENT'S IMMEDIATE PREGRAVID WEIGHT STATUS	NO. OF SINGLE BIRTHS	NO. OF INFANTS OF SPECIFIED BIRTH WEIGHT (POUNDS)				PER CENT OF INFANTS OF SPECIFIED BIRTH WEIGHT			
		TOTAL 2.3-5.5	5.1 TO 5.5	4.6 TO 5.0	2.3 TO 4.5	TOTAL 2.3-5.5	5.1 TO 5.5	4.6 TO 5.0	2.3 TO 4.5
Total	654	49	27	13	9	7.5	4.1	2.0	1.4
Overweight 20 per cent or more	99	4	2	1	1	4.0	2.0	1.0	1.0
10 – 19 per cent	71	4	2	2	0	5.6	2.8	2.8	0.0
+9 to –5 per cent	264	15	10	2	3	5.7	3.8	0.8	1.1
Underweight 6 – 19 per cent	193	20	12	5	3	10.4	6.2	2.6	1.6
20 per cent or more	27	6	1	3	2	22.2	3.7	11.1	7.4

Weight Change in First Trimester.—

Fig. 7 demonstrates that there was a very significant association between weight loss in the first trimester and the frequency of premature labor. Of especial interest is the fact that the premature labor rate does not decrease until the average gain of 3 pounds or more is reached. Again there is evidence that not only adequate but early prenatal care is imperative prior to the end of the first trimester. Any dysfunction, such as nausea and vomiting, can increase the probability of premature labor, and unless these dysfunctions, together with other evidence of nutritional deficiency, are recognized and corrected early the patient has an increased probability of catastrophe.

Weight Change in Second Trimester.—

When weight gain from the first visit to the clinic to 24-26 weeks is considered, Table V, there is a similar association between failure to gain at the

normal rate and the occurrence of premature labors. Weight change is tabulated according to the pounds more or less than the normal gain for the observed period of weeks.

TABLE V. FREQUENCY OF PREMATURE LABOR ACCORDING TO WEIGHT CHANGE FROM FIRST VISIT 24 TO 26 WEEKS' GESTATION, PATIENTS 30 PER CENT OR MORE OVERWEIGHT NOT INCLUDED

POUNDS MORE OR LESS THAN NORMAL GAIN	NO. OF BIRTHS	NUMBER OF PREMATURES			PER CENT OF BIRTHS PREMATURE		
		TOTAL	5 POUNDS, 1-8 OUNCES	5 POUNDS OR LESS	TOTAL	5 POUNDS, 1-8 OUNCES	5 POUNDS OR LESS
Total	602	48	26	22	8.0	4.3	3.7
5 pounds + more	73	1	0	1	1.4	0.0	1.4
3-4 pounds more	89	4	3	1	4.5	3.4	1.1
0-2 pounds more	173	11	4	7	6.4	2.3	4.0
1-2 pounds less	104	12	9	3	11.5	8.7	2.9
3-4 pounds less	84	11	7	4	13.1	8.3	4.8
5 pounds + less	79	9	3	6	11.4	3.8	7.6

The relative difference in these rates for premature labor is about the same as that found for weight change in the first trimester, i.e., about 12 per cent for those gaining less than normal average and a sharp drop to about 6 per cent at the average gain or better. Again, the drop in the premature rate does not occur until average, or better, gain is attained. Marked failure to gain 5 pounds or more less than average is associated strikingly with smaller premature infants.

Weight Change in Second Trimester for Patients With Different Gains in First.—

When weight gain or loss in the first trimester and that in the second trimester are considered independently, it is evident that the premature birth rate was lower among those patients whose gain in weight was average or more, than among those whose gain in weight was less than average. In Fig. 8 the patients are classified according to their weight change in these two periods of pregnancy.

Those who failed to maintain an average or better gain in weight during the second trimester, although their previous gain had been normal, had a premature labor rate of 7.3 per cent compared with 3.9 per cent for those who had average or better gain in weight throughout both periods. Thus, the premature labor rate was *75 per cent higher* when patients with early normal gain failed to continue to have average or better gain.

The relation of gain in weight during the second trimester to the premature labor rate is shown more strikingly for patients whose gain in the first trimester was less than average. If the gain in weight after attending clinic to 24-26 weeks of gestation was average or better, only 6.1 per cent of the patients had premature labors; but if the gain in weight continued to be less than average, 15.3 per cent had premature labors. This rate is approximately *150 per cent higher.* When a normal rate of gain was established at the time the patient came under supervision, the premature labor rate was not significantly higher for those with early weight loss, or less than average gain, than for those with average gain in the first trimester. However, less than average gain in *both* the *first* trimester and *second* trimester was associated with a premature labor rate two or more times greater than for patients with average gain or better in either the first or second trimester.

Pregravid Weight Status of Patients and Weight Gain to 24-26 Weeks.—

Since the premature labor rate is greatly affected by the immediate pregravid weight status of the patient, it is of interest to examine the relationship of gain in weight in the first two trimesters to the premature labor rates for women of different pregravid weights. This is shown in Table VI.

FIG 7	PREMATURE LABOR ACCORDING TO GAIN IN WEIGHT DURING FIRST TRIMESTER	
CHANGE FROM PREGRAVID WT. TO 12-16 WKS.	NO. OF PTS.	PERCENT OF PATIENTS HAVING PREMATURE LABOR
GAINED 6 POUNDS OR MORE	161	3.7%
GAINED 3-5 POUNDS	153	6.5%
GAINED 1-2 POUNDS	113	11.5%
FAILED TO GAIN OR LOST 1-2 POUNDS	84	11.9%
LOST 3 POUNDS OR MORE	91	9.9%

The variation in premature labor rates with difference in gain in weight is very similar for patients who are of standard weight or overweight, and for patients more than 5 per cent underweight. Those with average gain or better in both the first and second trimesters had the lowest premature labor rate; but even in this category the patients who were underweight had twice the frequency of premature labors as did the other patients.* Failure to show average gain in weight during the second trimester was associated with an increased premature labor rate; and if this failure followed a less-than-average gain, or loss, in the first trimester the premature labor rates became very high, 11.6 per cent for patients who were normal weight or overweight, and 24.4 per cent for those underweight.

There is a suggestion in these data that normal and overweight patients who have some weight loss, or below average gain in the first trimester, can have the probability of premature labor greatly reduced if normal gain in weight is established during the second trimester, but that underweight patients with early failure to gain have a relatively high probability of premature labor even though the gain in weight becomes normal during the second trimester.

Weight Change in Third Trimester.—

The relation of the gain in weight in the weeks following 24-26 weeks of gestation to the frequency of premature labor is shown in Table VII. The gain in weight after 24-26 weeks of gestation does not show a definite association with the occurrence of premature labor. However, there is a suggestion

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*For 68 patients whose pregravid weight was more than 5 per cent below the standard for their height and who gained 3 pounds or more above the average weight gain to 24-26 weeks, the premature birth rate was 2.9 per cent.

TABLE VI. PREMATURE LABORS ACCORDING TO PREGRAVID WEIGHT OF PATIENTS AND WEIGHT GAIN IN THE FIRST TWO TRIMESTERS OF PREGNANCY

GAIN TO 12-16 WEEKS	GAIN FIRST VISIT TO 24-26 WEEKS	PATIENTS 5 PER CENT UNDERWEIGHT TO 29 PER CENT OVERWEIGHT			PATIENTS MORE THAN 5 PER CENT UNDERWEIGHT		
		NO. OF PATIENTS	PREMATURE BIRTHS NO.	PREMATURE BIRTHS %	NO. OF PATIENTS	PREMATURE BIRTHS NO.	PREMATURE BIRTHS %
Total	Total	382	22	5.8	220	26	11.8
	Average gain or more	190	5	2.6	145	11	7.6
	Less than average	192	17	8.9	75	15	20.0
Average gain or above	Total	191	7	3.7	123	9	7.3
	Average gain or more	111	3	2.7	93	5	5.4
	Less than average	80	4	5.0	30	4	13.3
Below average gain	Total	191	15	7.9	97	17	17.5
	Average gain or more	79	2	2.5	52	6	11.5
	Less than average	112	13	11.6	45	11	24.5

TABLE VII. FREQUENCY OF PREMATURE LABORS ACCORDING TO WEIGHT GAIN TO 24-26 WEEKS' GESTATION AND FROM 24-26 TO 36-38 WEEKS

GAIN TO 24-26 WEEKS FROM FIRST VISIT	GAIN FROM 24-26 WEEKS TO 36-38 WEEKS*	NO. OF PATIENTS	PREMATURE BIRTHS %	PREMATURE BIRTHS NO.
Average gain or more	Total	335	16	4.8
	Above average, 4 pounds +	62	4	6.5
	Average to 3 pounds above	133	5	3.8
	Below average, 1 to 3 pounds	86	3	3.5
	Below average, 4 pounds +	54	4	7.4
Less than average	Total	267	32	12.0
	Above average, 4 pounds +	47	7	14.9
	Average to 3 pounds above	80	7	8.8
	Below average, 1 to 3 pounds	79	10	12.7
	Below average, 4 pounds +	61	8	13.1

*Difference from average gain for specific weeks that patient was observed is computed. For premature labors, the difference is to the last visit; and for about one-third of the patients, the last visit was before 36 weeks of gestation.

that the premature labor rate is increased for those patients who had average or better weight gains up to 24-26 weeks of gestation when either excessive gain, or a marked failure to gain in weight, occurred in the third trimester. On the basis of the number of patients available, the differences in premature labor rates for excessive gain, or failure to gain, and for patients with nearly normal gain in weight are not statistically significant.

Anemia and Premature Labor.—

It is not surprising that anemia, with its attendant anoxia, should have a direct effect on the incidence of premature labor. This represents a definite added stress which can affect the organism in many directions. The effect of anoxia on adrenal cortical function may have a direct bearing on the institution of premature labor, and may well represent one of the trigger mechanisms associated with its onset. The interrelation between adrenal cortical function and protein and carbohydrate metabolism, and the necessity for adequate protein levels to maintain normal uterine status have been established. Since anoxia is one of the primary stress factors which can affect adrenal cortical function, it is at least provocative that marked anemia, with the resultant anoxia, should have a direct bearing on the factor or factors incident to the onset of spontaneous premature labor.

In studying the relationship of anemia, or low hemoglobin levels, to premature labor, we must take into account the rapid drop in these levels which occurs during the first half of pregnancy as the result of increased plasma volume. Even the first hemoglobin value is affected, in most cases, unless it is obtained by eight or nine weeks of gestation. Therefore, we have classified hemoglobin levels by weeks of gestation, and the distribution of values obtained at any week was subdivided into four groups:

The highest 25 per cent, the middle 50 per cent, and the lowest 25 per cent, which was again subdivided to show the lowest 10 per cent.

Among patients classified according to their earliest hemoglobin value (all were obtained at 16 weeks or earlier), the premature labor rates among patients with different levels are shown in Fig. 9.

For all patients combined, the premature labor rate rises as the hemoglobin level decreases. This increase in rate, however, is not statistically significant until the lowest 10 per cent level is reached. Among patients in the lowest 10 per cent classification, the premature labor rate increases to 13 per cent, and this rate is statistically significantly higher than for all other hemoglobin levels combined.

Anemia, Immediate Pregravid Weight of Patient, and Incidence of Premature Labor.—

Low hemoglobin levels determined at the first visit to the research clinic occurred with about equal frequency among those patients who were underweight, and those who were of standard weight or above. Of the 430 patients whose immediate pregravid weight ranged from overweight to 5 per cent underweight, 29 per cent were in the low hemoglobin group. Among those 5 per cent or more underweight, 218 patients, 31 per cent, were in the low-hemoglobin group. The premature labor rate among patients classified according to their immediate pregravid weight status and their initial hemoglobin values is shown in Table VIII.

TABLE VIII. FREQUENCY OF PREMATURE LABOR FOR PATIENTS OF DIFFERENT IMMEDIATE PREGRAVID WEIGHT STATUS, AND WITH DIFFERENT INITIAL HEMOGLOBIN LEVELS

HEMOGLOBIN GROUP AND WEIGHT CLASS*	ALL PATIENTS			WHITE PATIENTS		
	NO. OF PATIENTS	PREMATURE		NO. OF PATIENTS	PREMATURE	
		NO.	%		NO.	%
Overweight to 5 per cent underweight	430	23	5.3	335	11	3.3
Hb. high 25 per cent	115	4	3.5	96	2	2.1
Hb. middle 50 per cent	191	11	5.8	153	6	3.9
Hb. low 25 per cent:						
a. 11-25 per cent	68	3	4.4	46	1	2.2
b. low 10 per cent	56	5	8.9	40	2	5.0
Underweight more than 5 per cent	217	26	12.0	171	15	8.8
Hb. high 25 per cent	53	5	9.4	44	3	6.8
Hb. middle 50 per cent	96	9	9.4	80	7	8.8
Hb. low 25 per cent:						
a. 11-25 per cent	39	7	17.9	28	3	10.7
b. low 10 per cent	29	5	17.2	19	2	10.5

*Height was not obtained for about the first 100 cases.

For the standard and overweight patients, the premature labor rate is lower for each hemoglobin group than for the underweight patients, and the strong association between weight status and prematurity is again shown. However, for both weight classes an increase in premature labor occurred among patients with low hemoglobin values. This increase did not appear, however, for the standard

and overweight patients, until the lowest 10 per cent hemoglobin is reached. At this level, the premature labor rate became 8.9 per cent, compared with 4.8 per cent for all women above the low ten per cent hemoglobin level. Among women

FIG 8	PREMATURE LABOR ACCORDING TO GAIN IN WEIGHT DURING FIRST AND DURING SECOND TRIMESTER		
GAIN IN WT. TO 12-16 WEEKS	GAIN FROM FIRST VISIT TO 24-26 WKS.	NO. OF PTS.	PERCENT OF PATIENTS HAVING PREMATURE LABOR
AVERAGE GAIN OR MORE	AVERAGE GAIN OR MORE	204	3.9%
	LESS THAN AVERAGE GAIN	110	7.3%
LESS THAN AVERAGE GAIN	AVERAGE GAIN OR MORE	131	6.1%
	LESS THAN AVERAGE GAIN	157	15.3%

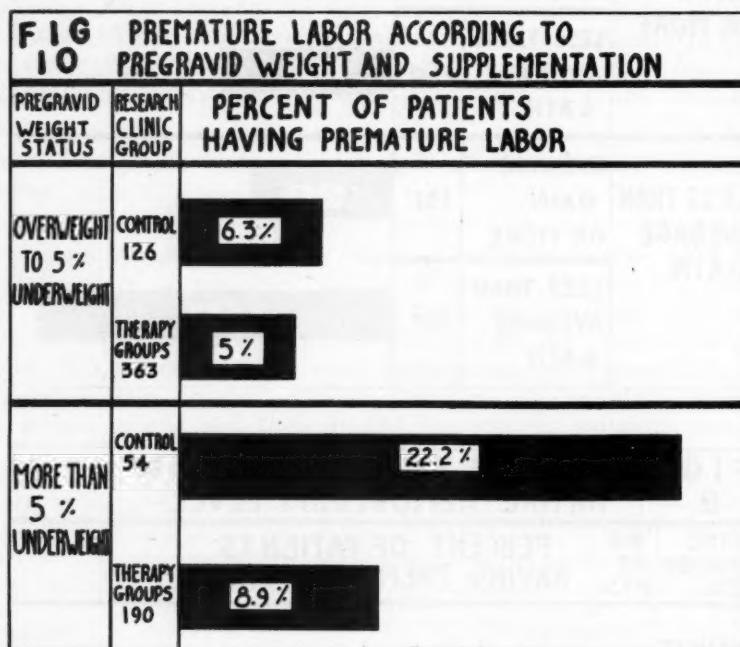| FIG 9	PREMATURE LABOR ACCORDING TO INITIAL HEMOGLOBIN LEVEL	
INITIAL HEMOGLOBIN LEVEL	NO. OF PTS.	PERCENT OF PATIENTS HAVING PREMATURE LABOR
HIGHEST 25%	202	5.4%
MIDDLE 50%	339	7.1%
LOWEST 25% 11-25%	121	8.3%
LOWEST 10%	91	13.2%

more than 5 per cent underweight, the premature labor rate increased at the low 25 per cent hemoglobin level, and is about 18 per cent for patients with values below this 25 per cent limit as compared with 9 per cent premature labor

when the initial hemoglobin was above the low 25 per cent level. Similar differences with hemoglobin levels are shown by the premature labor rates for white women only.

Thus, initial anemia is associated with an increase in premature labor, and when patients were both underweight and anemic, the premature rate is strikingly high.
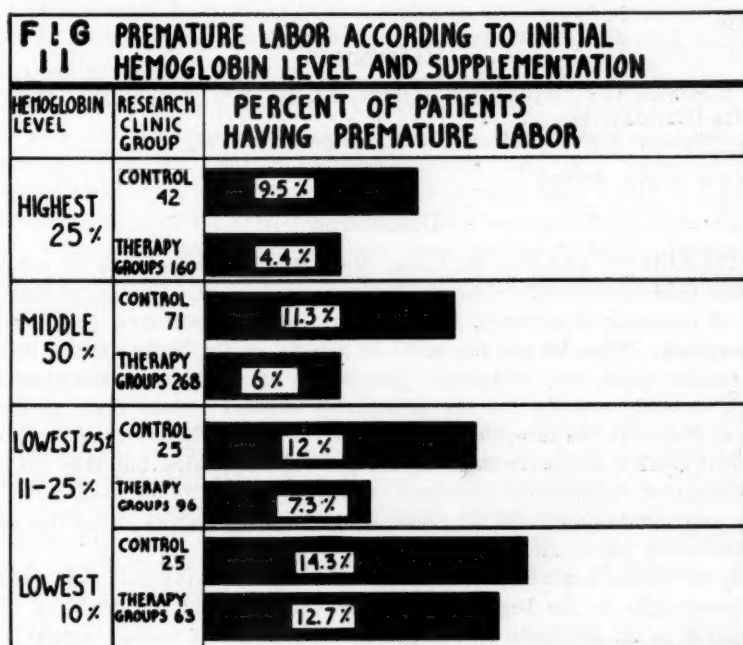
Premature Labor and Supplementation.—

One of the criteria of benefits to patients taking nutritional supplements is the premature labor rate. Fig. 10 considers the frequency of premature labor in relation to immediate pregravid weight among patients in the control and supplemented groups. Striking differences are apparent, and, here again, a marked difference occurs between the underweight and overweight patients. In addition,

FIG 10 PREMATURE LABOR ACCORDING TO PREGRAVID WEIGHT AND SUPPLEMENTATION

one very striking feature should be noted—that an essential difference does not occur in the rates among the control or therapy groups in patients who were standard weight or above. However, among the patients who were more than 5 per cent below standard weight at the beginning of pregnancy, the control group had a rate of premature labor of 22.2 per cent as against 8.9 per cent for comparable patients receiving supplementation; this or a greater difference would be expected from chance alone only once in 100 times. This again indicates the importance of the nutrient reserve factor among these individuals, and suggests that supplemental therapy has been effective only among patients underweight.

The relation of hemoglobin levels of patients to their response to supplementation is considered in Fig. 11. Among the control patients, the premature labor rate is about the same at all hemoglobin levels, but for patients who took supplements, the rate increases as the hemoglobin level decreases. Mothers in the lowest 10 per cent hemoglobin group who received supplements have a premature labor rate similar to that for the control group. Although the groups are small, this suggests that the supplements have been effective, or protective, for patients

who did not have anemia, but have had little or no influence when anemia was present, or was the dominant factor. If the experience with our control group of patients is typical, then in a general population not treated for nutritional deficiencies other than anemia, if it is so considered, the premature labor rates would not vary with hemoglobin levels, and anemia alone would not have an apparent association with premature labor. Thus, it is only when the other deficiencies are treated that the significance of the anemia as such appears. It is possible that the anemia per se has nothing to do with premature labor but that some underlying condition is responsible for both the anemia, which was a pregravid anemia, and the tendency for these patients to go into premature labor. As previously indicated, it may be that the anoxia associated with anemia and its effect on certain vital areas become the additional stress factor which is not commensurate with the safe conduct of pregnancy.

FIG 11 PREMATURE LABOR ACCORDING TO INITIAL HEMOGLOBIN LEVEL AND SUPPLEMENTATION

HEMOGLOBIN LEVEL	RESEARCH CLINIC GROUP	PERCENT OF PATIENTS HAVING PREMATURE LABOR
HIGHEST 25%	CONTROL 42	9.5%
	THERAPY GROUPS 160	4.4%
MIDDLE 50%	CONTROL 71	11.3%
	THERAPY GROUPS 268	6%
LOWEST 25% 11-25%	CONTROL 25	12%
	THERAPY GROUPS 96	7.3%
LOWEST 10%	CONTROL 25	14.3%
	THERAPY GROUPS 63	12.7%

Summary

In correlation of the causal relationship between nutritional deficiencies and toxemia and premature labor, it is apparent that a delicate balance exists in the pattern of gain in weight throughout pregnancy.

It has been shown that an approximately normal gain in weight during the first two trimesters is necessary to preclude the hazard of toxemia; and that an excessive restriction in the rate of gain during this period seriously increases the probability of premature labor—that a failure to gain at a normal rate during the first two trimesters must not be compensated for during the latter part of the second trimester in an attempt to avoid premature labor. Such a procedure then moves the patient directly into the zone of increased probability of toxemia; and the incidence of severe pre-eclampsia and eclampsia increases almost proportionately to the rate of gain in weight during this period.

There is no direct association between the incidence of toxemia and the incidence of premature labor. The pattern of premature labor is established by an initial underweight status of a patient, and/or her failure to gain at an acceptable rate during the first two trimesters. The mechanism for pre-eclampsia or eclampsia is established by an excessive gain during the second trimester, and continued into the third trimester—thus it is superimposed on the pattern for premature labor, and is not part of that pattern.

Since all patients exhibit some degree of deficiency, the management of this problem becomes one of re-establishing or maintaining a status commensurate with the added nutrient demands of pregnancy. Since the scale measures only added pounds and does not differentiate the nature of the gain, it is imperative that the weight increment be derived from specified nutrient intake and supplementation.

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Discussion

DR. WILLARD M. ALLEN, St. Louis, Mo.—Dr. Tompkins is to be congratulated on the careful and painstaking work which he has presented to us. Studies of this type require a good deal of planning in advance, a competent team of assistants, and, most important, constant supervision. That he has succeeded in this is amply borne out by the specific and informative results which were obtained. Not many of us, had we the time or facilities, would embark on such a study for the presumably obvious reason that we already believe women in good health at the inception of pregnancy will fare better than those who are not. His observations confirm the correctness of the general impression but they go much farther and raise some rather fundamental questions regarding our attitudes toward the management of pregnancy and our explanations for some of the accidents which occur during pregnancy, especially premature labor and toxemia.

Certainly no special comment needs to be made regarding the fact that patients who are 20 per cent overweight at the beginning of pregnancy show an incidence of 6 per cent of toxemia compared to an incidence of 1.7 per cent for those of normal weight. However, it is precisely in this category where he finds a dissociation between the complications of premature labor and of toxemia. In this group there is no increase over the normal of premature labor. Now when we look to the opposite group of patients, those who were 20 per cent or more underweight at the inception of pregnancy, the incidence of both toxemia and premature labor is considerably increased. In fact, this latter observation is one of the very worth-while contributions obtained from this study. I do not believe that many of us were aware of this prior to the presentation of this paper.

The net result to be gained from these correlations pertaining to prepregnancy weight as an index of health and, perhaps more important, as an index of body type, is simply that some of the complications of pregnancy have their origins in physiologic states existing prior to pregnancy. Prenatal care should then begin prior to the pregnancy. The overweight can be reduced and the underweight can be brought to normal, but it remains to be shown that these maneuvers in calories prior to the inception of pregnancy will decrease the incidence of prematurity and toxemia. Sober thought will make it obvious that the controls cannot be run.

The other fundamental correlations are more in the nature of confirmation of current thought, namely, that an excessive gain or inadequate gain are mild harbingers of trouble. However, I gather that Dr. Tompkins will have no sympathy with those of our clan who advocate markedly subnormal gains. Yet I am sure he is well aware of the excellent results

which some obstetricians report who actually starve their patients calorically. But we must remember that the advocates of this regime accomplish their aim by utilizing a high-protein, low-calorie diet.

Finally, I think his observation that a protein and vitamin supplement markedly decrease the incidence of toxemia and prematurity should settle the question once and for all regarding the need for careful consideration of the diet in the management of pregnancy.

We may ask ourselves, why do women gain 20 per cent of their body weight during pregnancy. It is obviously due to eating, but why do their appetites increase? The answer to this probably is to be found in the effect of the sex steroids on metabolic processes. For example, removal of the fetus in rabbits halfway through pregnancy does not stop the pregnancy. The placentas are delivered at term, as was shown by John Hammond more than thirty years ago; also, monkeys, as shown by Van Wagenen, deprived of their fetuses but retaining the placenta, continue to gain in weight and then lose the excess weight after the placenta is delivered at term. We may ask ourselves, then, may not failure to gain normally be a manifestation of abnormal functioning of the placenta, and may not the abnormal placenta be in part due to an unfavorable environment in the early weeks following implantation?

DR. FRANK E. WHITACRE, Memphis, Tenn.—I have had an opportunity to make some observations that I think support Dr. Tompkins' thesis. As you know, we most commonly see the most severe toxemias in indigent patients. In a series of consecutive cases of eclampsia seen in China, all were in indigent patients; and in a series of 100 cases of eclampsia seen in a charity hospital in Memphis, all of them were in the indigent class. At the private hospitals, most of the eclamptic patients had been admitted to the charity service. Climate, race, color, and geographic location seem to make little difference—the only common factor was that most patients were in the indigent group, who could be expected to have nutritional deficiencies.

DR. EDWARD L. KING, New Orleans, L.—I would like to ask Dr. Tompkins to explain what form of vitamin therapy and protein therapy he uses.

DR. TOMPKINS (Closing).—The vitamin supplement used in the Research Clinic is a polyvitamin concentrate of therapeutic potency. Initially an arbitrary level of dosage was established with the hope that this arbitrary level would demonstrate a differential, if such a differential could be demonstrated, when compared to the control group.

As is graphically shown in Fig. 5, this was not demonstrated in the number of patients studied to date, and we have also found that in a large number of patients, the level used has been insufficient to protect tissue status.

The protein supplement is a concentrate essentially vitamin and mineral free. This supplies 50 Gm. of protein, as a supplement, and this level was also established arbitrarily in an effort to evaluate the possibility of added protein being the causative factor in the improvement in maternal nutrition which we had previously observed. Again because of the number of patients studied to date, a clear-cut differential has not been established.

All research study groups are given the same basic diet which contains 65 Gm. of protein to which supplements are added. This diet is for investigational purposes only and it must not be interpreted as a recommended level of dietary intake of protein in that it is definitely below desirable levels. It is used for differential purposes only when the various groups are compared.

Vitamin therapy, which we have found essential, is an individual problem and must be based on individual patients' needs as reflected by tissue status. In general, however, it will be found that the need for supplemental vitamin therapy is much greater than previously considered. Supplemental protein therapy is not the procedure of choice in that high biologic protein from dietary sources is more efficient, protective, and no more expensive.

OVARIAN PREGNANCY*

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IN ANY discussion on ovarian pregnancy, first we must admit that such a state exists, second, abide by the established standards that determine the pathology.

It is necessary to make it clear that we envisage here only those pregnancies that are primarily of ovarian origin. It is possible to encounter them as secondary to tubal abortion, but these must not be taken into consideration when discussing ovarian pregnancies as such.

It is difficult to understand why a great number of cases of this variety of ectopic pregnancy have been reported in the medical literature, that are definitely not of ovarian origin. As long ago as 1876, Hueppe,[1] in an inaugural dissertation, established the necessary conditions to consider a pregnancy as of ovarian origin: "1) fecundation on the ovary, the ruptured follicle closing itself afterwards, and the fetus developing in the interior of the ovary as a cyst; 2) the ruptured follicle does not close itself but the placenta retains its implantation in the ovary."

Ten years later, Werth[1] analyzed the characteristics of ovarian pregnancy, concluding that "there is only one positive variety, and that its value for the anatomical diagnosis is of the utmost importance: it is when the fetal sac is manifestly ovarian in origin and that the state of the Fallopian tube excludes the possibility of its participation in the formation of the fetal sac."

Pozzi,[3] in 1897, discussed thoroughly the views of his predecessors and contemporaries on this subject, and mentions but 11 cases that were acceptable to him: "Many reported cases," he writes, "are tubo-abdominal pregnancies secondarily implanted on the ovaries."

Diagnoses in those days were mostly established by gross pathology. The study of histological specimen with the microscope was still in its infancy.

It was Spiegelberg who formulated the four conditions, now generally accepted, as indispensable to determination of the ovarian origin of a pregnancy. These are: "(1) that the tube, including the fimbria ovarica, be intact and the former clearly separate from the ovary; (2) that the gestation sac definitely occupy the normal position of the ovary; (3) that the sac be connected with the uterus by the ovarian ligament; and (4) that unquestionable ovarian tissue be demonstrable in the walls of the sac."

In accepting these conditions, it is indispensable that we cast aside the outmoded theories that the ovum has to submit to some maturation changes within the fimbria or the tube to possess the power of being fertilized by the spermatozoa; or that the escape of the egg from the follicle might be retarded by a tortuous channel of exit or that, after rupture of the follicle, the ovum might be retained within the discus proligerus, according to the teaching of Leopold.[5]

But we must admit that the secretion of the corpus luteum is essential for implantation (not necessarily within the follicle from which the ovum was discharged), and that the great frequency of the presence of endometrium in the ovary favors the nidation of the egg within the cortex. Even so, in many cases it is very difficult, if at all possible, to determine the method of implantation.

Clinically it is nearly impossible to diagnose the condition. In the early stages it does not differ from any uterine or tubal pregnancy. Authors have elaborated considerably to establish the diagnosis of ovarian pregnancy; yet there are no specific symptoms permitting a positive statement in the matter. Even in the study of the evolution of the pregnancy, if the origin of the ectopic may be suggested, no proof of it can be established until all the factors enumerated above can be traced.

Eden and Lockyer[6] write that "nothing resembling a tubal abortion can take place in an ovarian pregnancy." This is in clear contradiction to other authors; on the other hand, when we consider that the ovarian tissue is susceptible of expanding a larger sac than the tubal tissue, it is not surprising to read of a certain number of cases of ovarian pregnancies going to full term.[7] A term gestation in a tube is a rarity. In an ovary it is proportionately much greater. In such cases, a diagnosis of ovarian cyst is usually made. Ruptures of ovarian pregnancies happen frequently when the fertilized ovum is implanted superficially.

Sutton, cited by Wollner,[8] considers the superficial type as a secondary ovarian pregnancy, in which the ovum "following its fertilization undergoes a certain stage of its development in some near-by structure or cavity, and then becomes implanted in the ovary." This is a debatable point of view. It eliminates all pregnancies whose development is traced to the cortex of the ovary, those that are more likely to rupture.

When rupture occurs, the similarity of symptomatology between tubal and ovarian pregnancies makes it definitely pure guesswork to formulate a diagnosis. The rarity of ovarian origin naturally induces us to speak of ectopics with the tubal variety in mind. Hematocele is generally to be found in Douglas' pouch, although in one of our cases it developed into the broad ligament. Some hesitation was then experienced in definitely formulating a diagnosis of ruptured ectopic pregnancy. The puncture of Douglas' pouch was negative. The Aschheim-Zondek test is done routinely in such cases, although we do not give it more importance than it merits, especially when it is not positive.

Even at the time of operation, the gross examination cannot permit a certain diagnosis. Simard[9] does not hesitate to formulate the possibility that "a number of observations reported as ruptured corpus luteum with peritoneal inundation are early ovarian ruptured pregnancies. The presence of trophoblastic elements in the tissues of a corpus luteum is the evidence of a pregnancy. The fecundation of the ovum at the cortex of the ovary at the site of the follicular rupture is generally the rule. Hemorrhage appears rapidly, the very young embryo is drowned and lost in the flow of blood, and a few placental elements are all that persist at the surface of the ovary to certify the pregnancy." The great majority of ovarian pregnancies rupture at such an early stage that it is often impossible to recognize embryonic elements by sight. The histological examination is indispensable in formulating a diagnosis, and, moreover, it gives precise information as to the exact location of the ovular nidation.

"It has been recognized," states Lecène,[10] "that there exist two types of ovarian nidation: in the corpus luteum itself (which corresponds to a fertilization of the ovum in the Graafian follicle before the rupture), and outside the corpus luteum. . . . There do not generally exist decidual cells in the ovarian stroma in the vicinity of chorionic villi."

Moulonguet[11] reports 77 authenticated cases of ovarian pregnancy. Yet in his study of these cases, there are no less than 18 that the author himself classifies as doubtful or definitely not of ovarian origin, or with insufficient data to be acceptable scientifically. In the rupture or stay of early ovarian pregnancies, the embryo disappears rapidly by autolysis and therefore it is the pregnancy which has to be demonstrated. In the well-developed pregnancy, the ovarian tissue disintegrates and it is the ovary that has to be found again.

These are the problems which confront the pathologist in his search for a microscopic diagnosis.

We operated upon a patient with ectopic pregnancy which was diagnosed as of ovarian origin by the pathologist. Discussion following the joint study of the operative protocol and more sections examined proved it not to be the case. This and another case which is a true ovarian pregnancy are here reported. In reviewing the files at our Hospital for the past 30 years, I could trace only two cases, one already published by Simard,[9] and the one I will report. Four other cases I rejected on the ground of insufficient data, and had them reclassified.

In reporting these two cases taken from the University of Montreal, Department of Gynaecology, Notre-Dame Hospital, I had in mind to show the necessity of closer cooperation between the pathologist and the gynecologist, to determine definitely the origin of an ovarian pregnancy.

CASE 1.—Mrs. M. G., 42 years of age, was admitted in January, 1949, with the complaint of heaviness in the lower abdomen for the last 10 months, gradually more and more apparent. There was also noted a nearly continuous loss of blood, by spotting and otherwise, from April to September, 1948. She had amenorrhea in September and October. Since November, intermittent hemorrhages reappeared with leucorrhea during the intervals. She had had 10 pregnancies, 5 at term, 1 premature, and 4 miscarriages. Her last confinement occurred 17 years ago in 1932. Her last miscarriage was in April, 1948. Examination showed the presence of a tumor bulging 4 cm. above the pubis, regularly shaped, median, partly mobile and painless. The vulva and vagina were normal. The cervix was small, with a transverse opening, regular, mobile, hard. The body of the uterus was hard, the size of a large melon, filling the entire pelvis and bulging up to 4 cm. above the pubis. The cul-de-sac was free and painless.

The provisional diagnosis was that of a fibromyoma of the uterus. The Aschheim-Zondek test was negative. There was a slight degree of anemia, 3,375,000 red cells, and 65 per cent hemoglobin. The white count was normal. A laparotomy was decided upon.

Upon the opening of the abdomen, a large cystic left ovary, the size of a grapefruit, was located in the broad ligament. It was multiloculated with yellowish liquid in some regions, reddish in others.

The right adnexa were marked by intimate adhesions with the omentum and the small intestines. Once they were liberated, we found a hard voluminous mass of dark yellowish tint, adherent to the posterior peritoneum. The uterus was slightly enlarged and adherent posteriorly to the rectosigmoid.

It was decided to proceed with the total hysterectomy and right adnexectomy. Then the intraligamentary cyst was removed.

Upon opening of the right adnexal mass, which was the ovary, the tube being adherent to it, but not included in the tumor process, a fetus was dislodged by the pressure of a large blood clot (Fig. 1).

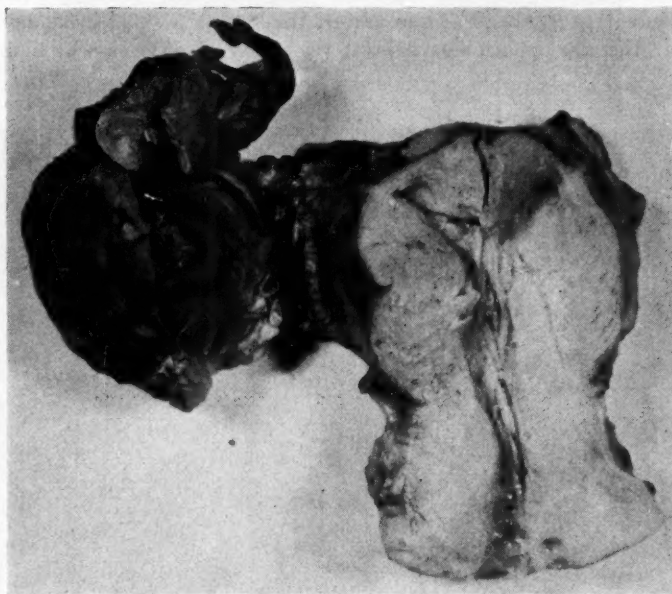The histological specimens confirmed the ovarian origin of the pregnancy as shown in Figs. 2, 3, 4, 5, and 6.

Fig. 1.—The fetus is displaced from the ovary by manipulations.

Fig. 2.—Showing the relation of the ovarian tissue, the tube, and the clot.

CASE 2.—Mrs. N. G., 27 years of age, was admitted to the Hospital on Nov. 11, 1950, for acute abdominal pain in the right iliac fossa that started 6 days previously, preceded the night before by some slight reddish discharge, becoming darker gradually, with a tendency to disappear, and progressively increasing pains. Vomiting had been present for the last 24 hours only. She had had splitting headaches during the week.

Leucorrhea had been noted since the last confinement 5½ months ago and amenorrhea since the confinement. She had had 5 pregnancies, 3 full term, 1 premature, and 1 miscarriage at 4½ months. The last pregnancy ended June 21, 1950. The miscarriage was back in 1942.

The patient traveled to Montreal by car from her country home. Upon arrival at the Hospital at 7:10 P.M. she complained of severe pain in the abdomen. She was anxious; pulse 95, blood pressure 130/80. Palpation did not reveal the rigid tension of an "acute abdomen." A painful mass was found in the right iliac fossa. Dark blood and clots in small quantity were noted. The cervix was hard and closed. The fundus of the uterus was 2 cm. above the pubis, anteflexed, mobile and painful. The right cul-de-sac was very painful, filled with an oval-shaped mass adherent to the body of the uterus, the size of a small cucumber. The left cul-de-sac was free. Douglas' pouch was painful yet empty of any mass or liquid. A puncture was negative.

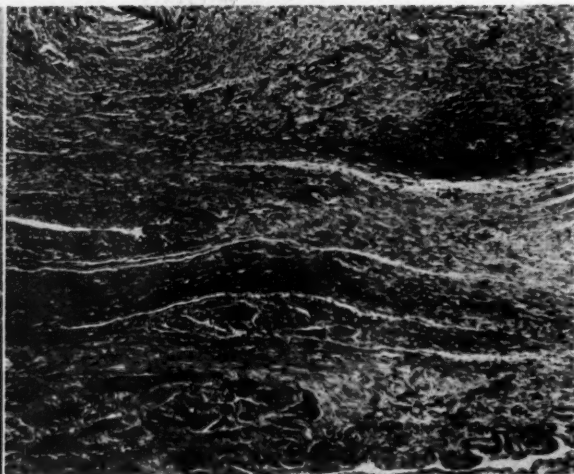Fig. 3.   Fig. 4.

Fig. 3.—At low power showing the darker streaks of ovarian tissue, the lumen of the tube and the clot.
Fig. 4.—At high power the darker streaks of ovarian tissue are more apparent.

The blood count showed 3,300,000 red cells but a 96 per cent hemoglobin. The white count was normal.

Before the Aschheim-Zondek report (which was very weakly positive), the patient developed another acute attack and immediate operation was decided upon with the tentative diagnosis of: (a) unruptured right ectopic pregnancy, or (b) twisted, right ovarian cyst.

Upon opening of the abdomen, the right iliac fossa was walled off by the omentum, and its liberation revealed an encysted collection of blood, intimately linked with the ovary; the tube appeared intact. The mass was removed in its entirety including the ovary, the tube, and the clot. The left adnexa and the uterus were normal.

A report from the pathologist read, ". . . the tube is intimately adherent to the ovary; it is in sub-acute inflammatory reaction and contains liquid in its lumen. The ovary contains a large clot in which are found placental villi partly necrotic. Apparently, we are facing an ectopic pregnancy of ovarian origin." This report made me rush to the laboratory with the file of the patient and we were shown (Fig. 7) a slide with ovarian tissue above a large clot and the tube intimately linked with both the clot and the ovary.

A fragment of the clot was taken in a region presumably at the cortex of the ovary showing characteristic villi, but no surrounding or attached ovarian tissue was found. More sections were made but nowhere were we able to confirm an original liaison between the ovary and the villi.

We therefore declined to approve the pathological report as exact and, in the light of my explanations, the report was rewritten.
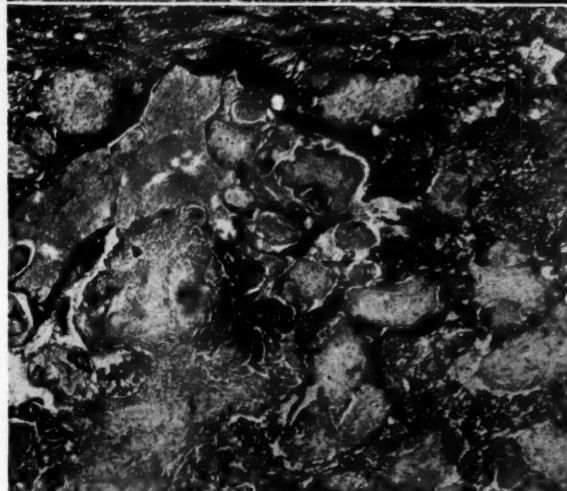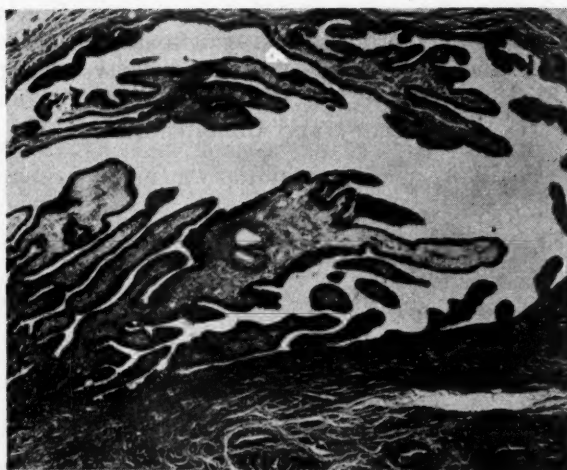
Fig. 5.

Fig. 6.

Fig. 5.—At high power the normal appearance of the fimbria is evident.

Fig. 6.—Chorionic villi are numerous in the clot as could be expected in a pregnancy as far advanced.
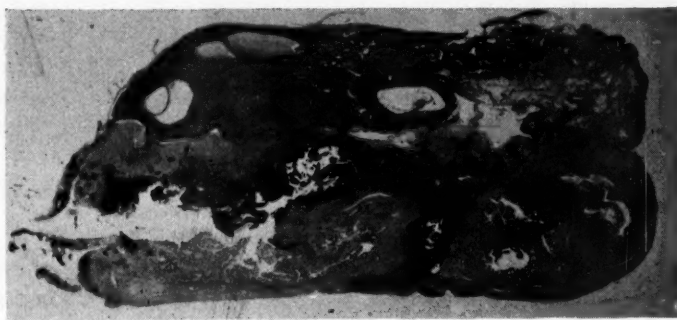

Fig. 7.—Showing the relation of the three tissues, ovary, tube, and clot.

We are prone to ask too much with too little from the pathologists. They must possess satisfactory data to ensure a true examination and report. This applies to all specimens, but more so perhaps in suspected cases of ovarian gestation where the operative protocol must be clear, precise, giving a correct picture of the findings.

Summary and Conclusions

Outmoded methods by gross examination of specimens of presumably ovarian pregnancies should be discarded.

Histological findings are insufficient to prove the origin of an ovarian pregnancy.

Close cooperation of the pathologist and the gynecologist is indispensable to the solution of this difficult problem.

Two cases are reported to demonstrate these contentions.

I wish to thank Dr. Raymond Simard, one of my associates, for allowing me to publish one of his cases.

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Discussion

DR. ARTHUR HERTIG, Boston, Mass.—It is with great pleasure that I discuss Dr. Gerin-Lajoie's thorough review of this rare but important abnormality of pregnancy. It comprises 0.7 to 1.07 per cent of all ectopic pregnancies. At the Free Hospital for Women we have had 110 ectopic gestations, one of which[1] was of primary ovarian type, or an incidence of 0.91 per cent, a figure in agreement with those of other authors. Its absolute incidence (based on 1 in 300 pregnancies being ectopic) is thus of the order of one for each 25,000 to 40,000 pregnancies.

The essayist has properly emphasized the near impossibility of correctly diagnosing the condition preoperatively. Such pregnancies are thought to be either ordinary tubal pregnancies (if the history is suggestive of an ectopic gestation at all) or an ovarian cyst with or without a twisted pedicle. The chorionic gonadotropic hormone tests and endometrial curettage are likewise equivocal, as in ordinary ectopic pregnancies.

The etiology of these rare ectopic implantations of the fertilized ovum is unknown. Dr. Gerin-Lajoie has correctly pointed out that the ovum, to be capable of fertilization, does not have to mature in the oviduct. Indeed, Dr. Rock[2] and I have shown in a paper on human ovulation, published in this JOURNAL during 1944, that the follicular egg undergoes mitosis as part of the reduction division process in preparation for its subsequent fertilization.

Since the mechanism of transporting the normally ovulated ovum from the peritoneal cavity to the fimbriated end of the tube is obviously not perfect, it is not surprising that

such an ovum ("wrecked upon the peritoneal wastes," according to Irving) should occasionally meet a wandering spermatozoon which has strayed from the safe seclusion of the oviduct. It then becomes a matter of pure chance as to whether these two lost gametes, now happily made one zygote, remain in the follicle of origin, implant on the peritoneum, or make a delayed entrance into the Fallopian tube.
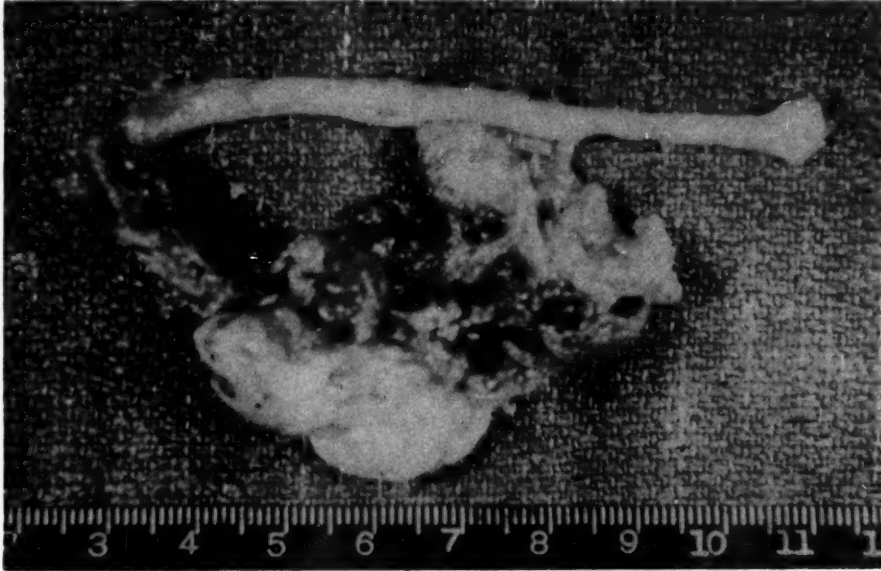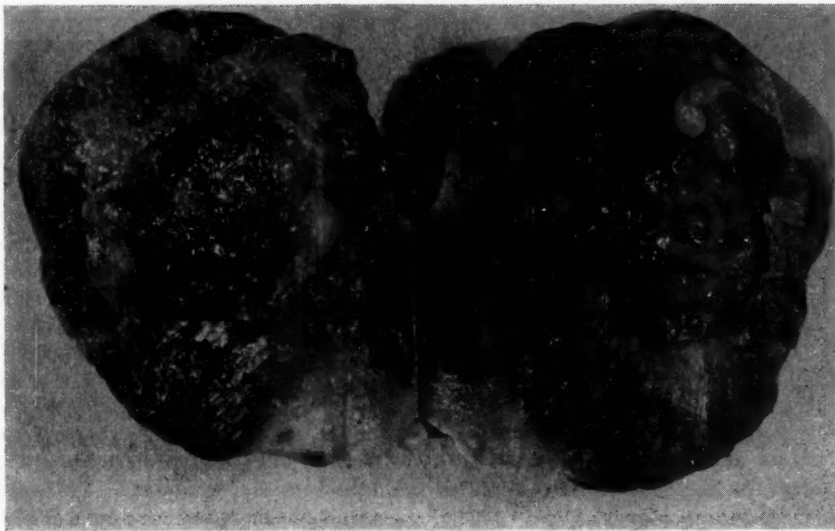

Fig. 1.

Fig. 2.

I doubt whether the presence of pseudodecidua in the ovary has anything to do with the causation of ovarian pregnancy. One need only remember that all ovaries of pregnant women have such tissue which blossoms under the stimulus of the rising amounts of estrogen and progesterone. - Moreover, tubal pregnancies rarely have any such ectopic decidua-like tissue, granting that decidua is the critical factor in implantation of the fertilized ovum, which I doubt. Normal implantation occurs during the twentieth day, or 6 full days after

ovulation, when the normal endometrium is in the edematous phase prior to the formation of decidua. Last, endometrium is not necessary to implantation of the ovum since the rare, complete placenta accreta is implanted on myometrium pathologically devoid of endometrium.

The pathological diagnosis of ovarian pregnancy is not without its pitfalls as has also been stressed by the author. One can do no better than to emphasize the criteria laid down by Spiegelberg in 1878. I shall take the liberty of showing three slides that illustrate 3 out of these 4 diagnostic criteria (Figs. 1, 2, and 3).

Fig. 3.

Fig. 1 shows a recent ovarian pregnancy from Dr. John Parks' Clinic at the George Washington University Hospital. I am indebted to Dr. R. Barter for his kindness in allowing me to use this specimen which shows an intact normal tube in the presence of an ovary which microscopically was the seat of an ectopic gestation.

Fig. 2 shows a bisected ovary completely surrounding an intact ovisac of 3.7 cm. in greatest diameter containing a 14 mm. stunted, macerated embryo attached to a 4 mm. umbilical cord. The associated Fallopian tube was negative. The interest attached to this Boston Lying-in Hospital case (No. 23243, S-37-676) is because the patient, a gravida iii, para ii, with one normal and one dead erythroblastotic infant, complained of lower quadrant pain during the fourteenth week of a normal intrauterine pregnancy. The preoperative diagnosis, based on a soft, tender, movable mass the size of a lemon in the left vault, was a left ovarian cyst complicating a normal 3½ months' gestation. At operation the specimen shown in Fig. 2 was removed following which the patient made an uneventful convalescence. She subsequently delivered by the breech a 6 pound, 10½ ounce baby who suffered from erythroblastosis of the icterus gravis type but recovered following transfusion. This case, here recorded for the first time, constitutes the rare heterotopic gestation associated with normal intrauterine pregnancy. Up to 1937 there were 74 such cases but only 4 of them were of combined ovarian and intrauterine pregnancy.

Fig. 3 illustrates the microscopic proof of an ovarian pregnancy, namely, the juxtaposition of normal chorionic tissue and ovarian substance; in this instance, the corpus luteum itself. I am indebted to Dr. Howard Ulfelder of the Massachusetts General Hospital for his kind permission to cite this case (MGH No. 717304). Aside from the excellent histologic criteria of ovarian pregnancy shown in the specimen, the chief interest in this case lies in the gross appearance of the right ovary at the time of operation. It was interpreted as a bleeding corpus luteum which was resected with good restoration of normal ovarian anatomy. The gross diagnosis was correct but it was also an early ovarian pregnancy associated with the

corpus luteum. Of interest is the fact that the patient subsequently became normally pregnant and is due to be delived in August, 1951.

This case illustrates the point made by the essayist when he quotes Moulonguet to the effect, "In the rupture or stay of early ovarian pregnancies, the embryo disappears rapidly by autolysis and, therefore, it is the pregnancy which has to be demonstrated. In the well developed pregnancy, the ovarian tissue disintegrates and it is the ovary that has to be found again."

In summary, may I thank Dr. Gerin-Lajoie for his excellent presentation, and for the opportunity to discuss three additional cases which illustrate the significant criteria of primary ovarian pregnancy?

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DR. FREDERICK H. FALLS, Chicago, Ill.—I have had only one ovarian ectopic pregnancy in my experience. It was a case in the Cook County Hospital on the service of Dr. Kobak, who made the diagnosis of ectopic pregnancy and operated upon the patient. After he came out of the operating room he handed me the specimen and said, "I operated for an ectopic pregnancy but found a bleeding ovarian cyst, probably a corpus luteum cyst." I told him that I was not so sure that it was a bleeding cyst and asked to have the specimen. Three days later we opened the specimen and saw a beautifully preserved intraovarian fetus with the placenta intact. I report this particularly because I believe that this is the best way for us to preserve such valuable material. If we open the specimen in the operating room we are too likely to mutilate it and thus destroy in part its teaching value.

DR. ISIDOR C. RUBIN, New York, N. Y.—Ovarian pregnancy is not encountered by all of us. Very often a whole lifetime may pass without personally meeting with such a case. It is just fortuitous if one meets with an ovarian pregnancy, such as was the case in my own experience. In 1911 I came upon an ovarian pregnancy and recognized it only because I was associated with a gynecologic pathologic laboratory and was interested in the pathologic aspects of the lesions we met. About a year later Dr. S. W. Bandler had a patient who he thought had an ovarian pregnancy. The ovary was enlarged and bleeding and was occupied by a hemorrhagic mass. The tube looked perfectly normal. He removed the ovary and left three-quarters of an inch of the tube in but I insisted on his removing that little portion of the tube and, to be sure, that portion of the isthmus contained the conceptus, about 1.5 mm. in diameter. It was probably the youngest ectopic tubal pregnancy I have ever encountered. In other words, the tube must be removed with the corresponding ovary in order to establish whether or not the ovary is the seat of the pregnancy. Pseudo-ovarian pregnancy is not so uncommon. The lesions most commonly confused with ovarian pregnancy are ruptured hemorrhagic corpus luteum and chocolate cysts. If one has met a case of ovarian pregnancy he is more likely to look for it than anyone who has not seen a real case of such pregnancy. When I presented my first case, Norris had collected 19 cases. Some twenty-five years later I had another case of ovarian pregnancy where not only villi were present but the fetus. The report of this rare lesion is always timely.

DR. GERIN-LAJOIE (Closing).—I would like to thank the discussers for confirming my opinion on ovarian pregnancy. The cases which have been reported by Drs. Hertig, Falls, and Rubin are extraordinarily similar to the one I mentioned. The case was of a young unmarried girl who came into the hospital for an attack of acute appendicitis. At operation the appendix was found to be practically normal but on the ovary was a small clot with a piece of omentum adherent to it. A general surgeon removed the appendix and liberated the adhesions. The ovary started to bleed a little and he swabbed it. Bleeding continued and he swabbed it again, and then decided it would be better to remove that portion. This he did and it was sent to the laboratory and was found to be an ovarian pregnancy. The literature is difficult to evaluate. I believe there are many more such pregnancies than are reported and that a number of reported pregnancies of ovarian origin are not ovarian pregnancies.

A CLINICAL AND SURGICAL REVIEW OF ENDOMETRIOSIS*

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Rochester, Minn.

(From the Division of Surgery, Mayo Clinic and from the Mayo Foundation)

THIS review is a continuation of one which one of us (Counseller) presented before this Society in June, 1938. In that report cases encountered at the Mayo Clinic from 1923 through 1937 were reviewed. This study, being similar, covers the ten-year interval from 1939 through 1948. In these ten years 1,342 patients received surgical treatment at the clinic for endometriosis. This is approximately 25 per cent of the total number of cases of endometriosis encountered during this period. To state it another way, we can say that only 25 per cent of all of the patients presenting evidence of endometriosis were subjected to some type of surgical treatment; the remainder were treated medically.

The purpose of this study was to search for certain information or facts which would aid in the selection of treatment for these patients. In order to do this, it is necessary to inquire as to what changes took place in the menstrual cycle and what effect, if any, the previous surgical operations may have had; also, what influence did pain have in disability and, finally, when conservative operations were done, what were the effects, if any, on restoration of fertility and the relief of pelvic pain.

In a way, we wish to apologize for adding another paper dealing with the surgical treatment of this disease, but it may be helpful in establishing a unanimity of opinion in the management of this rather serious and disabling disease. Furthermore, this condition has almost replaced the common pelvic inflammatory disease of preantibiotic days. Since blood in the peritoneal cavity is irritating, it may be confused with inflammatory disease in its early stages. In this connection it is interesting to note that therapy, such as hot douches and vaginal diathermy, aggravate rather than relieve the symptoms of endometriosis, which is a distinguishing feature between endometriosis and pelvic inflammatory disease.

Age

There is probably more information contained in this factor than we are able to interpret at the present time. We have tried to illustrate the age at time of operation at the clinic in Fig. 1. The disease is present throughout the entire reproductive period of the woman's life and in some cases after the menopause. In our cases just about as many patients were less than 30 years of age as were more than 50 years of age. The greatest number of patients were between 30 and 50 years of age at time of operation at the clinic. This late development of this disease which requires surgical intervention could be due to delay in marriage and childbearing, to a slow natural growth of the endometrium and adenomas or to the physical status of the patients. Perhaps we

never will know for sure. The patients beyond the menopause who require surgical treatment for endometriosis usually have other surgical lesions or have degeneration of large adenomas of the uterus or obstructive lesions due to pelvic adhesions and inflammation. It should be significant that all the patients who are treated medically are usually less than 30 years of age and comprise 75 per cent of the total number of patients seen at the clinic. Should more of these patients be treated surgically, there would be a rather marked increase in the incidence between 20 and 30 years. I am sure that the younger group shown on the left-hand side of Fig. 1 need the best judgment concerning advice and therapy. The problem becomes easier to decide as the patient's age increases toward 45 years.
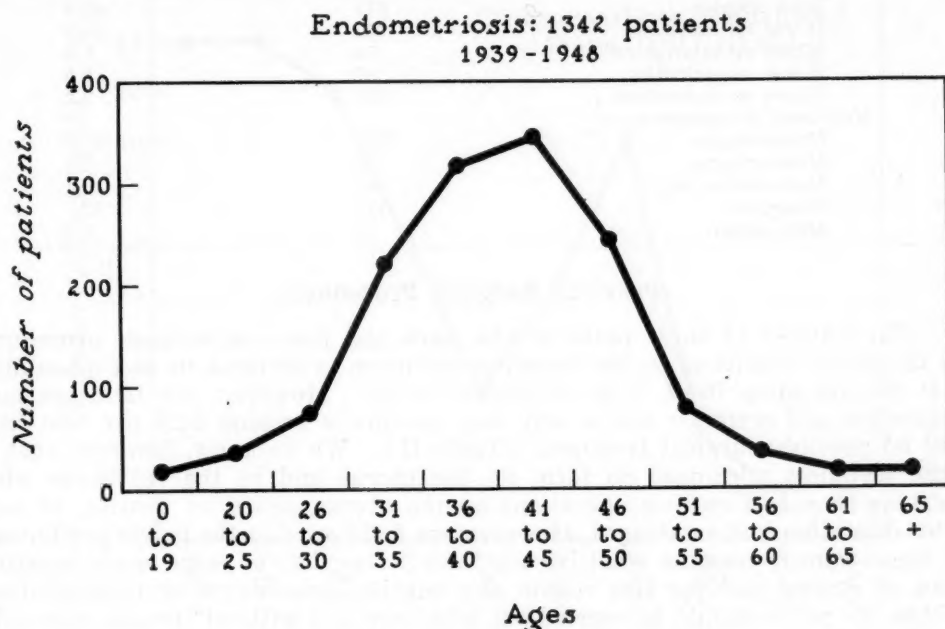

Fig. 1.—Age at time of operation.

Site of Lesions

The site of the lesions is always interesting and in this group the location was about the same as that described in previous communications. The majority of the lesions are on the uterus and ovaries and in the cul-de-sac. In this series of cases, however, there were 33 in which the bladder was involved, 169 in which the rectosigmoid was involved, and 11 in which the small intestine was involved. Furthermore, there were a few unusual locations such as the inguinal region, the cervix, and the vulva. Some lesions were seen in postoperative abdominal scars and in the umbilicus. Distant extensions to the extremities or to the chest were not seen.

Menstrual Abnormalities

It should be significant that 88.3 per cent of all patients had some type of menstrual abnormality, which was menorrhagia, metrorrhagia, menometrorrhagia, or simply irregular periods (Table I). Patients who do present these irregularities or abnormalities do not always have the characteristic pain of endometriosis. In this group a little more than half did not give any history of dysmenorrhea and this fact probably explains the large number of young

women who are treated medically and the small number who are treated by
conservative surgical procedures. The pain in some cases was worse on defeca-
tion, urination, exertion, and on sexual relations.

TABLE I. MENSTRUAL ABNORMALITIES: 1,342 PATIENTS

	NUMBER	PER CENT OF TOTAL CASES
Menstrual Abnormality.—		
Present	1,185	88.3
Absent	157	11.7
Total cases	1,342	100.0
Pain.—		
With menses	611	45.5
Worse on exertion	254	18.9
Worse on intercourse	74	5.5
Worse on urination	87	6.5
Worse on defecation	123	9.2
Menstrual Disturbances.—		
Menorrhagia	357	26.6
Metrorrhagia	102	7.6
Menometrorrhagia	260	19.4
Irregular	171	12.7
Menopausal	56	4.2

Previous Surgical Procedures

The number of these patients who have had previous surgical procedures
on the pelvic organs or on the intestine continues to intrigue us as a possibility
that the operation itself is an etiological factor. However, our data are only
suggestive and certainly not in any way conclusive because 53.8 per cent have
had no previous surgical treatment (Table II). We do know, however, that in
some instances adenomas do form on the uterus and in the cul-de-sac when
patients have had cutting operations on the uterus, tubes, or ovaries, or even
after dilatation and curettage. However, we do know that the pelvic peritoneum
of some women remains sensitive all their lives, that of some more sensitive
than of others, and for this reason any surgical procedures or manipulations
within the pelvis should be carried out with care and without trauma, especially
in the young person, who may exhibit some irregularity of the menses and
dysmenorrhea.

TABLE II. PREVIOUS SURGICAL PROCEDURES ON 1,342 PATIENTS LATER TREATED FOR
ENDOMETRIOSIS

	NUMBER	PER CENT OF TOTAL CASES
Previous Surgical Treatment.—	620	46.2
Involving cutting uterus, tube, ovary	377	28.1
Dilatation, curettage, and perineal operation	170	12.7
Appendectomy or other abdominal operation	276	20.6
No previous surgical treatment	722	53.8
Total	1,342	100.0

Diagnosis

Little needs to be said about the clinical diagnosis of endometrial lesions
except that this diagnosis is being made much more frequently before operation
than it was a few years ago. Certain symptoms, if present, should direct at-
tention to the possibility of endometriosis even though there may be other
associated lesions of the uterus and adnexa; for example, acquired dysmenor-
rhea of the progressive type occurring in a woman particularly between the

ages of 25 and 45 years. This stage will vary in character depending on the site of the lesion. Adenomatous lesions of the uterus not infrequently extend through and involve the posterior wall of the bladder. These lesions are illusive and hard to diagnose, and difficult to determine on cystoscopic examination. Most of them are suspected of being carcinoma but biopsy usually shows a benign lesion. The symptoms become exaggerated with menstruation and finally the pain continues throughout the entire cycle. Another characteristic of this
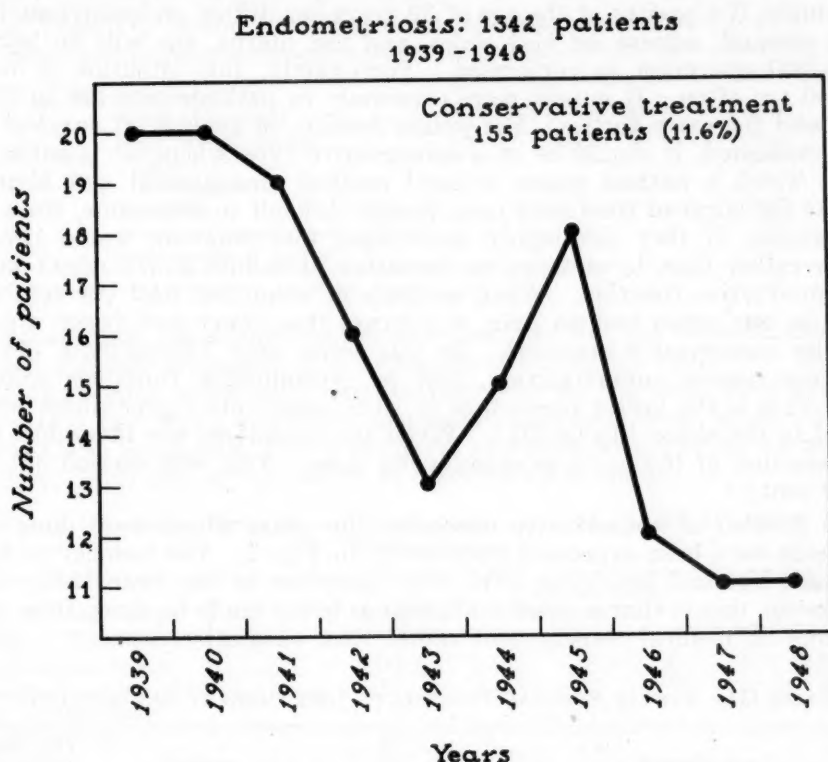

Fig. 2.—Number of conservative operations by years.

particular lesion is that rarely are there other lesions in the pelvis except the one involving the bladder and uterus. Just why this should be, it is impossible to interpret. These may lend themselves well to local excision. Pain on defecation or rectal pressure, which becomes exaggerated with the initiation of menstruation, is usually indicative of an endometrial lesion which disturbs the mucosa of the rectum or rectosigmoid. These lesions may be palpated by rectal examination. Rarely do they produce obstruction but they may extend into the lumen of the bowel and be palpated as spurs. Pelvic soreness which is brought about by exertion near or during menstruation is significant of endometrial lesions. In addition, if patients complain of sterility and they have rather pronounced dysmenorrhea, endometriosis must necessarily be excluded as an etiological factor. Another significant point in the diagnosis is that the tenderness or pain is usually out of all proportion to that seen in other pelvic lesions. This is particularly true if an examination happens to be made near the beginning of menstruation. Why these lesions should be so much more sensitive than other types of lesions in the pelvis is always an interesting question. It may be that these lesions are occurring in the pelvis which has been a sensitive one even before the lesions occurred.

Surgical Treatment

Surgical treatment consists of partial or complete removal of the pelvic organs. However, in some instances ovarian function may be saved when hysterectomy is done. In a few cases conservative procedures may be done with preservation of the reproductive function or the ovarian function or both. It seems to us that the extent of the lesions and their location are of more importance in selecting the type of operation perhaps than is the age of the patient. For example, if a patient at the age of 30 years has diffuse endometriosis involving the sigmoid, adnexa on both sides, and the uterus, she will be better off if a radical operation is performed. Fortunately, this situation is not encountered too often. It is seen more commonly in patients who are in the late thirties and the early forties. For young women, in general, if surgical treatment is indicated, it should be of a conservative type whenever possible. The point at which a patient ceases to need medical management and becomes a candidate for surgical treatment is extremely difficult to determine, since many young women, if they thoroughly understood the situation, would prefer to carry on rather than to undergo an operative procedure which might sacrifice their reproductive function. When we keep in mind that 54.5 per cent of the patients in our series had no pain, it appears that fewer and fewer are being treated by conservative measures. In this series only 155 patients (11.6 per cent) were treated conservatively, that is, reproductive functions were preserved. This is the lowest percentage of such conservative procedures we have ever had in the clinic (Table III). When the conditions are favorable, a presacral resection of the nerve is occasionally done. This was carried out on 13 (1.0 per cent).

The number of conservative operations by years which were done in the past decade have been expressed graphically in Fig. 2. The number so treated has become less and less since 1939 with exception of the year 1945; the explanation for this is that a greater attempt is being made to carry these young folks along on medical management rather than surgical treatment.

TABLE III. TYPE OF SURGICAL TREATMENT: 1,342 CASES OF ENDOMETRIOSIS

TREATMENT	NUMBER	PER CENT OF TOTAL CASES
Conservative.*—		
With presacral resection of nerves	13	1.0
Without presacral resection of nerves	142	10.6
Total	155	11.6
Radical.—		
Castration	670	49.9
Some ovarian function preserved	517	38.5
Total	1,187	88.4
Roentgen therapy (for recurrences of pain)	22	1.6
Radium therapy	1	0.1

*Operations preserving menstrual function.

Radical operations were done in 88.4 per cent of our cases with complete castration in 49.9 per cent and preservation of some ovarian function in 38.5 per cent (Table III). Occasionally, a part or almost all of an ovary which is free from any endometrial lesions can be preserved. This ovary can be preserved following either a subtotal or total hysterectomy even though there may be some endometrial lesions remaining in the cul-de-sac or on the bowel. The remaining lesions rarely produce trouble due to the preserved ovarian function.

Surgical Procedures.—The usual surgical procedures are listed in Table IV. Total abdominal hysterectomy was done 879 times, subtotal abdominal hysterectomy 135, and vaginal hysterectomy 139 times. The extent of the lesions and involvement of cul-de-sac and uterosacral ligaments determine for the most part what type of hysterectomy should be performed. When the cul-de-sac is free and hysterectomy is indicated, vaginal hysterectomy may be performed but it should be done with considerable caution with respect to any fixation of the bladder and rectum.

TABLE IV. SURGICAL PROCEDURES FOR ENDOMETRIOSIS: 1,342 PATIENTS

	NUMBER*
Hysterectomy.—	
Total abdominal	879
Subtotal abdominal	135
Vaginal	139
Other Procedures.—	
Excisions	199
Presacral resection of nerves	14
Suspension of uterus	19

*More than one procedure in some cases.

The surgical procedures which were used in the 155 cases in which conservative surgical measures were employed is shown in Table V. These may consist of excision alone or in combination with the various procedures listed. In 18 (11.6 per cent) a uterine suspension operation was done. When the cul-de-sac was reasonably free a presacral resection was done as an additional procedure. This was performed in 13 cases (8.4 per cent).

TABLE V. CONSERVATIVE SURGICAL PROCEDURES ON 155 PATIENTS TREATED FOR ENDOMETRIOSIS

PROCEDURE	TOTAL*	WITH UTERINE SUSPENSION	WITH PRESACRAL NEURECTOMY
Excision	71	7	2
Salpingo-oophorectomy	50	2	2
Oophorectomy	17	4	1
Partial oophorectomy	36	3	4
Tubal operation	21	1	
Myomectomy	38	1	4
Resection of bowel	3		
Dilatation and curettage	34		
Total		18 (11.6%)	13 (8.4%)

*More than one procedure in some cases.

Fertility

The question of fertility in endometriosis is of considerable importance. Much information can be obtained on this phase of the subject by studying the 155 patients on whom conservative surgical treatment was carried out. The information from a review of the fertility in these cases before any operation was done for endometriosis is given in Table VI. Thirty-four (21.9 per cent) of the patients were unmarried, 78.1 per cent were married. Of the married group, 68 (56.2 per cent) had no pregnancies. This is a much higher percentage of absolute sterility than we have found in our previous studies. Here, again, the explanation for this high percentage of sterility is based on the fact that patients are carefully selected for conservative surgical treatment and a higher percentage of these may have sought surgical relief from their sterility. Of those who did become pregnant, 15.7 per cent had 1 living child and 17.4 per cent had 2 or more living children. This group of 121 married patients among

whom pregnancy could reasonably be expected was not productive of children. A secondary sterility not uncommonly develops in patients who have endometriosis. They may never become pregnant the second time and, if they do, it not uncommonly results in miscarriage. In those patients with secondary sterility, the onset of the disease frequently dates back a short time subsequent to delivery, giving cause to believe that the pregnancy or delivery may have been an exciting factor in its production or that the pregnancy or delivery may have reactivated a pre-existing endometriosis. Miscarriages occurred in 10.7 per cent of cases.

TABLE VI. FERTILITY OF 155 PATIENTS BEFORE CONSERVATIVE SURGICAL PROCEDURES

STATUS	NUMBER	PER CENT
Unmarried	34	21.9
Married:	121	78.1
No pregnancies	68	56.2*
One pregnancy with living child	19	15.7*
Two or more pregnancies with living children	21	17.4*
Miscarriages only	13	10.7*

*Per cent of married women.

Following conservative surgical procedures, we were able to trace 75 patients (Table VII) for further study of their fertility problem. Of those who reported by letter or who have been seen subsequently in the clinic as return patients, 17 (22.7 per cent) were unmarried, 10 (13.3 per cent) were more than 40 years of age, leaving a group of 48 (64 per cent) in whom pregnancy might reasonably be expected. Eight women had been pregnant once, 1 woman became pregnant twice, and 1 became pregnant three times, one pregnancy of which resulted in a miscarriage. In all, there were 13 pregnancies, resulting in 12 living children.

TABLE VII. FERTILITY: 75 PATIENTS WHO WERE TRACED

PATIENTS	NUMBER	PER CENT
Unmarried	17	22.7
40 years of age or more	10	13.3
Reasonable expectancy of pregnancy	48	64.0

Of the 48 Patients With Reasonable Expectancy of Pregnancy			
TIMES PREGNANT	WOMEN	PREGNANCIES	CHILDREN
One	8	8	8
Two	1	2	2
Three	1	3*	2
Total	10†	13	12

*One miscarriage.
†Twenty and eight-tenths per cent of 48 patients.

Results of Conservative Surgical Procedures

In evaluating results obtained from conservative treatment, one must consider the degree of pelvic comfort obtained, whether the reproductive function was improved, and also whether further treatment for the endometriosis was required. The results are not particularly encouraging (Table VIII). Good results were obtained as far as relief of pain was concerned in only a fraction more than 60 per cent. The poor results are a little bit more impressive; that is, 22.7 per cent of the patients were not improved as far as relief of pain was concerned. Eight per cent of the patients required subsequent surgical treatment, 4 per cent required some roentgen treatment for relief of pain, and a smaller group was treated with hormone therapy. The results of restoration of fertility also, as said before, were disappointing.

TABLE VIII. RESULTS: 155 PATIENTS TREATED CONSERVATIVELY

	WITH PRESACRAL NEURECTOMY	WITHOUT PRESACRAL NEURECTOMY	TOTAL	
			NUMBER	PER CENT
Patients treated	13	142	155	
Traced	11	64	75	48.4*
Results: Relief of Pain.—				
Excellent	5	18	23	30.7†
Good	2	23	25	33.3
Fair	3	5	8	10.7
Not improved	1	16	17	22.7
Died	0	2	2	2.6
Subsequent pregnancy	1	9	10	13.3
Subsequent operations	0	6	6‡	8.0
Other Treatment.—				
Roentgen rays	0	3	3	4.0
Radium	0	0	0	0.0
Androgens	0	2	2	2.7
Estrogen	0	4	4	5.3

*Per cent of total patients treated conservatively.

†Per cent of traced patients.

‡2 hysterectomies; 2 excisions; 1 partial oophorectomy and plastic operation; 1 posterior colpotomy.

Comment

The purpose of surgical treatment is the relief of pain, the correction of irregular menstrual periods, the improvement of fertility in those patients who have been unable to become pregnant, and the correction or the prevention of miscarriages or stillbirths. the incidence of which is high in these patients. Obviously, the quickest and most certain way for the relief of pain is the destruction of the ovarian function, either by surgical removal of the ovary or by castration by radiation therapy. However, this is not advisable as a routine procedure, especially for young patients, particularly for those who are anxious to have a child or to have more children. Women who have had 1 or 2 or more children, whose paramount desire is relief of pain and the correction of menstrual periods, may be adequately taken care of by hysterectomy and perhaps the preservation of the ovarian function when the ovaries are uninvolved by the endometrial lesions. This is a very satisfactory procedure when it can be carried out since the patient has her family, she is relieved of pain, and she does not suffer from postmenopausal symptoms for a few years. Treatment must be individualized. The needs of one patient are not always the same as the needs of another.

In summing up the data herein presented, the problem seems to be one of selection of patients for surgical treatment. At the clinic we have reduced this problem to 25 per cent of all of the patients presenting evidence of endometriosis. Of this 25 per cent, the number of patients who are treated conservatively has been gradually reduced in the past ten years. The reasons for this seem obvious. In our hands, at least, the results do not justify the extension of surgical procedures to more young people. If we submitted more younger women to surgical exploration for endometriosis, we would secure some relief from pain, the possible correction of some of their menstrual irregularities, and possibly they would have some children after operation. It seems to us, however, that the same group of patients if they are treated medically, or have no treatment at all, would have just as many children and perhaps be just about as comfortable until they reached that age at which surgical treatment of a radical nature would be required either for the endometriosis or for associated lesions of the uterus and adnexa.

Our previous reports and those of others have shown that radical surgery is required for associated pelvic lesions by more than 50 per cent of patients who have endometriosis and are in the third or fourth decades of life. Our records in this group of cases show approximately the same percentage of associated lesions although they were not specifically listed. A repetition of this fact seems unnecessary. It seems clear to me that in surgical treatment the problems are so numerous that, if the patient elects to have surgical treatment, the surgeon should be privileged to do whatever procedures he deems justified, even to the extent of complete removal of all pelvic organs. For younger patients, if conservative procedures are feasible at the time of exploration, it should be his privilege to carry them out, but he should not make any promises in regard to the improvement of fertility. If a patient has had one or two miscarriages, the removal of a chocolate cyst or the correction of the position of the womb may permit a subsequent pregnancy under careful management to go to term. Our figures show that it is not possible to demonstrate that conservative procedures for sterility alone are of much value since only 10 patients (20.8 per cent) of the 48 patients, who could reasonably be expected to become pregnant, did subsequently do so. However, these 10 patients had 13 pregnancies and 12 living children. These are rather low figures to indicate improvement of fertility and on which to recommend operation for the primary purpose of correcting sterility. The probability of subsequent pregnancy without any surgical procedure seems to me to be equally as high and I am sure that I have observed that this does happen in a great many instances. The patient who has had one child and then who fails to become pregnant again may have a greater chance of improvement of her sterility by a surgical procedure than otherwise.

Presacral resection as a surgical procedure in this disease is, of course, reserved for those patients who are treated conservatively but we are doing it less and less because we doubt that it adds much to local excision of implants, especially if a unilateral excision of adnexa is added. Furthermore, I rather feel that the opening of the posterior peritoneum to attack the presacral nerve may carry certain disadvantages in that subsequent implants may develop in the line of the suture. We performed presacral neurectomy only thirteen times in this group of 155 patients.

Resection of the intestine usually is not necessary in those cases in which all of the ovarian tissue has been removed since the lesion, if it is producing obstruction, will usually be absorbed sufficiently to relieve the obstruction. When conservative procedures are carried out resection of the bowel may be indicated, and it was done three times in this group of patients. Resection of the bowel is not the dangerous operation that it was in the preantibiotic days so that the surgeon need not hesitate if the indications for such resection are present. When radical operations are performed, and there is a lesion of the sigmoid or rectosigmoid, the surgeon must be certain that the lesion is an adenomyoma and not a silent carcinoma of the bowel. When the patient who clinically seems to require radical surgical treatment has definite symptoms referable to the bowel a roentgenogram of the colon is of value. It is especially indicated for older patients since roentgenographic examination of the colon will help differentiate between a benign and a malignant lesion of the bowel. The adenomyoma does not disturb the mucosal pattern of the intestine as does the malignant lesion. If roentgenologic examination of the colon has not been done and the situation is encountered at the time of operation, a specimen should be removed very deep from the lesion for biopsy. If this is benign, nothing further needs to be done with it if the ovarian tissue is going to be removed, unless there is marked obstruction. If marked obstruction is present, a temporary colonic stoma is of value.

Although radical operations were done in 88.4 per cent of our patients, complete castration was carried out in 49.9 per cent, while ovarian function was preserved in 38.5 per cent. The preservation of ovarian function whenever possible in this disease, I think, is a useful procedure and only 1.6 per cent had to have any subsequent roentgen therapy for recurrences of pain. The younger the patient on whom radical surgery is done, the greater the effort to preserve this function.

Hormone therapy has been used sparingly for the relief of recurrent pain after conservative treatment, and it has not been used clinically for the relief of pain to the extent that it has in some other institutions. It has been shown that female sex hormones in large doses can cause leucemia in mice. Leucemia is a malignant disease of the blood cells. Therefore, large dosages of female sex hormones must be considered as carcinogenic. Thus we seriously doubt whether use of a substance which may be carcinogenic for the relief of a benign lesion can be justified. Estrogens were given to 2.6 per cent of our patients who were treated conservatively and androgens to 1.3 per cent.

Summary and Conclusions

In the ten years from 1939 through 1948 surgical treatment has been used at the Mayo Clinic for 1,342 patients, or approximately 25 per cent of the patients who were given a diagnosis of endometriosis or who were suspected of having this condition. In the majority of these 1,342 cases, endometriosis and its associated lesions of the uterus and adnexa seemed to require radical surgical treatment for the relief of symptoms. This was done in 88.4 per cent of the cases, although ovarian function was saved in 38.5 per cent. Conservative operations should perhaps be limited to those patients who are less than 30 or 35 years of age and have a combination of disabling pain, irregular menses, and sterility sufficient to require surgical interference. Conservative procedures cannot be recommended for the correction of sterility although they should be carried out whenever possible in the hope that fertility may be restored during the reproductive period of life. It perhaps should be considered especially for those patients who have pelvic lesions in addition to the endometriosis, have had one child, and are anxious to have subsequent pregnancies. Failures will occur in the group of patients who have absolute sterility. Finally, the selection of patients for surgical treatment is the critical issue. It will depend in many instances on the associated pelvic lesions which of themselves require surgical treatment. Patients who have these are usually in the older age group. Operations on the younger patients probably should be determined by the degree of disability and without any definite promise of relief or improvement in their sterility.

Discussion

DR. RICHARD Te LINDE, Baltimore, Md.—This paper of Dr. Counseller's has interested me greatly and will serve to help us crystallize our ideas about this disease which apparently is occurring with greater frequency. Dr. Scott and I have recently made a similar study of our cases covering a period of fifteen years and I have been interested in comparing our findings and conclusions with those of Dr. Counseller. As to age and menstrual abnormalities, our studies in general are in agreement with his. We are also in agreement that although pain is the commonest symptom, there are many cases of endometriosis that are not accompanied by pain. In our series there were 26.9 per cent who were without any pain. Although dysmenorrhea of some type was present in about 80 per cent of our cases, the textbook pic-

ture of acquired dysmenorrhea was present in only 9 per cent. Also there was no dysmenorrhea of any kind in 16 per cent of our cases. The point I wish to make is that endometriosis and even extensive endometriosis may be present without pain and without dysmenorrhea.

The most important question that Dr. Counseller evaluates has to do with the selection of cases for surgery and the type of surgery done. He has pointed out that at the Mayo Clinic in recent years there has been a tendency to defer surgery for some time but to do radical surgery when the patient actually comes to it. He does not believe that his results justify conservative surgery for the relief of sterility alone. Although it is difficult to make any rules regarding surgery in this disease, I believe the following, much of which is in agreement with Dr. Counseller and some slightly divergent, is sound. I do not believe that it is justifiable to explore the pelvis on the basis of a history of acquired dysmenorrhea and other symptoms suggestive of endometriosis when the pelvic findings are negative. If you do so, you will generally be disappointed in finding no evidence of the disease. In such cases we find culdoscopy very convenient.

In a young woman complaining of sterility who has palpable endometriosis and who has been unsuccessfully attempting pregnancy for at least two years, I believe laparotomy is justifiable, even though not indicated on the basis of relief of pain. I take this view on the basis of our results. Sixty-four of our married patients who were operated upon conservatively and who desired children were followed from nine months to fifteen years. Twenty-six became pregnant and there was a total of 38 pregnancies; 31.8 per cent of the women had term babies. This is a higher percentage than was reported by Counseller but perhaps some of our cases of lesser degree of endometriosis would not have been operated upon by him and would have become pregnant without surgery. To state concisely my views regarding conservative surgery on young women I would say that I believe in doing surgery relatively early while conservative surgery is still possible. I agree with Dr. Counseller that a great many women with endometriosis whose symptoms are not sufficiently severe do not require surgery. In the fourth decade I believe hysterectomy with preservation of at least some ovarian tissue is often the operation of choice. I judge that Dr. Counseller agrees with me in this for he states that some ovarian tissue was saved in 38.5 per cent.

Dr. Counseller performed vaginal hysterectomy 139 times and states that he does this by choice when the cul-de-sac is free. Although I have encountered endometriosis in doing vaginal hysterectomy through error, I believe laparotomy is the approach of choice when the diagnosis is made preoperatively.

DR. EMIL NOVAK, Baltimore, Md.—With rare exceptions operations for endometriosis should be based on palpatory findings rather than mere symptoms. There is a tendency, especially on the part of the general surgeons who do such a large part of the gynecologic surgery in this country, to assume that a woman with dysmenorrhea of the acquired type probably has endometriosis, even though pelvic examination is negative. Under such circumstances, laparotomy will usually not reveal endometriosis. If it shows a tiny ''implant'' or two on the ovary, the surgeon has no right to feel impressed, as the implant probably had nothing to do with the symptoms.

Endometriosis is not always associated with pain or even appreciable discomfort. We all see patients in whom, because of such findings as uterosacral nodules, we feel sure that endometriosis is present, and others in whom residual endometriosis is present after previous operation, and yet such patients get along indefinitely with little or no discomfort. There is usually no more justification for operation in such cases than there is in the numerous patients who obviously have long-standing chronic pelvic inflammatory disease with little or no symptomatology. Endometriosis is rarely a life-endangering disease, and carries with it almost no cancer hazard. As a rule, such patients should be treated expectantly in the hope that pregnancy will occur, as it not infrequently does.

On the other hand, the disease is of course a distressing one in many patients, and operation is often necessary. Dr. Counseller has strongly and properly stressed the desirability of conservative operations in women in whom later childbearing is hoped for, and hence I was surprised that in 88 per cent of his cases the operations were of radical type, a proportion far higher than my own.

DR. J. P. PRATT, Detroit, Mich.—One more point in favor of conservatism might be added to this discussion. We have an unusual opportunity to observe patients who have endometriosis. In all patients who come to the Henry Ford Hospital for general physical examination, it is our practice to have one of the gynecologists check the pelvis. That gives us a great opportunity to see any patients with pelvic complications, including endometriosis. There are many patients who have endometriosis, according to physical findings, yet do not have any pelvic complaints. Frequently they come back later and still have no pelvic complaints. During many pelvic operations, lesions of endometriosis, varying in size, are noted. A careful check of patient's history after operation gives no indication that they had any symptoms due to these lesions. So we know there are many patients who carry this condition without symptoms. It seems to us that a note of conservatism should be emphasized and that we should be sure of the symptoms of endometriosis. I am sure Dr. Counseller has seen endometriosis at the time of operation for something else without any indication that the endometriosis had given symptoms.

Another thing I would like to know is how often is this condition progressive? In the group of patients we examine from time to time, we find that the lesion is about the same year after year. I believe, generally, endometriosis tends to be an episode and does not progress.

DR. WALTER DANNREUTHER, New York, N. Y.—I would like to ask two questions: What are Dr. Counseller's indications for the supplementation of the pelvic operation with presacral neurectomy, and what is Dr. Counseller's impression regarding the necessity for repeat operations for endometriosis in patients followed up for a period of five to twenty years?

DR. CONRADO ZUCKERMANN, Mexico City, Mexico (by invitation).—Five years ago the problem was a topic for discussion at the Gynecological Section of the National Assembly of Surgeons at the Juárez Hospital, and I was asked to present the etiology of endometriosis as part of this symposium. One thing I was able to determine was that this condition seems to be less frequent in Mexican Indian women. I attribute that to the fact that less surgery is performed on them; they are more fertile, have fewer abortions, and as a rule therefore, have large families.

DR. THADDEUS MONTGOMERY, Philadelphia, Pa.—I should like to use the opportunity to secure information concerning a problem in endometriosis which has proved troublesome to me on several occasions. I am referring to endometriosis of the vaginal vault, rectovaginal septum, and posterior cul-de-sac in which there is a rather extended local lesion which gives rise to bleeding, painful intercourse, and dysmenorrhea, but in which the internal genitals appear to be involved to only a limited degree.

In such situations I have found it difficult to eliminate the disease by excision of the involved areas in the vaginal vault or by elimination with local radiation therapy, and yet I have felt loath to ablate the relatively uninvolved uterus and ovaries in order to depress endometrial activity.

I wonder if Dr. Counseller has any suggestions as to the handling of this rather difficult and compromising situation.

DR. COUNSELLER (Closing).—Dr. Te Linde has raised the question of vaginal hysterectomy; I think he is entirely right about the selection of the approach. If the operation is performed specifically for endometriosis, it should be done as an abdominal operation. In the 135 cases in which vaginal hysterectomy was done, there were some nodules in the cul-de-sac of Douglas or perhaps there was a chocolate cyst, the existence of which had not been known before operation, and the real indication was for vaginal plastic work.

It pleases me that Dr. Novak mentioned the large number of times that radical surgery has been used. I think I can clarify that. We are not using radical surgery in all cases of endometriosis. Many patients had conditions of the uterus and adnexa which required radical operations. Still others had extensive endometriosis for which, primarily, they did not undergo operation; they were included in this series because of the endometrial lesions,

although half of them had fibroid tumors with lesions of the adnexa which needed attention. Hence, in the over-all group, radical surgery was employed rather often, but for differing reasons.

Dr. Pratt asked if endometriosis is progressive. Actually, I cannot answer that question. I think that in many cases the condition remains about the same. If the patients proceed without too much trouble into the menopause they may not need surgical treatment. On the other hand, in some of them the condition does not become quiescent.

Dr. Dannreuther asked about recurrence of the lesion over a period of five to twenty years. That is a good question. I believe that some patients with endometriosis do not require surgical treatment, but, if they do, I believe it probably is required because of associated pelvic lesions rather than endometriosis itself, unless a large adenoma is present which will undergo a certain amount of degeneration due to interference with the blood supply. In that type of case the patient may require surgical treatment after an interval of twenty years. We are using presacral neurectomy less and less frequently. I believe the patient not thus operated on does just about as well as the patient who has undergone this operation. Occasionally, when pain is severe and we have employed conservative surgical treatment in an effort to save reproductive function, and where there have been lesions in the cul-de-sac, we may do presacral resection and carry out some type of suspension of the uterus. I believe we must keep in mind the fact that the pelvic peritoneum of patients who have endometriosis is different from the peritoneum in the rest of the abdomen. It must be handled more carefully than the peritoneum in the upper part of the abdomen; if it is not, the consequence may be a tremendous number of endometrial implants in the pelvis. I have seen implants in the peritoneum of patients who had undergone presacral neurectomy, an occurrence which causes me to hesitate somewhat in regard to performance of presacral resection. However, when pain is paramount, presacral neurectomy is a valuable procedure.

Dr. Montgomery has brought out the question of lesions in the rectovaginal septum. I agree that such a condition is a difficult problem. It just happens that a few days before I came here a young woman, who eighteen years ago had had a very extensive lesion in the rectovaginal septum which I considered inoperable, came back for examination. She had undergone radiation therapy, and to the time of this report she has been entirely free of pelvic complaints. Her pelvis is in excellent condition. She is now 51 years old. She returned because of recurrent pain. She had been told elsewhere that she had carcinoma of the ovary, but I am convinced that she does not have it. Why some of these lesions become sensitive after the menopause is, I think, a problem which warrants investigation. I reassured this patient and sent her home.

I hope I have not misled you into thinking that we are performing a great many radical surgical operations for this type of lesion, because I do not believe we are.

(The paper of Dr. Curtis J. Lund read at this meeting will appear in the November issue.)

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. (1876) *President,* Walter T. Dannreuther, New York. *Secretary,* John I. Brewer, 104 South Michigan Ave., Chicago, Ill. Next meeting, Hot Springs, Va., May 12, 13, and 14, 1952.

American Association of Obtetricians, Gynecologists and Abdominal Surgeons. (1888) *President,* Leroy A. Calkins, Kansas City, Kan. *Secretary,* William F. Mengert, 2211 Oak Lawn Ave., Dallas 4, Texas. Annual meeting Hot Springs, Va., September 11, 12, and 13, 1952.

Central Association of Obstetricians and Gynecologists. (1929) *President,* Russell J. Moe, Duluth, Minn. *Secretary-Treasurer,* Harold L. Gainey, 116 S. Michigan Ave., Chicago 3, Ill. Annual meeting to be held in September, 1951.

South Atlantic Association of Obstetricians and Gynecologists. (1938) *President,* E. D. Colvin, Atlanta, Ga. *Secretary-Treasurer,* John C. Burwell, Jr., 416 Jefferson Bldg., Greensboro, N. C.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Arthur B. Hunt, Rochester, Minn. *Secretary,* Bernard J. Hanley, 1930 Wilshire Blvd., Los Angeles, Calif. Annual meeting, Chicago, Ill., June 9-13, 1952.

New York Obstetrical Society. (1863) *President,* Howard C. Taylor, Jr. *Secretary,* Charles M. McLane, 960 Park Ave., New York 28, N. Y. Second Tuesday, from October to May.

Obstetrical Society of Philadelphia. (1868) *President,* James P. Lewis. *Secretary,* George A. Hahn, 255 S. 17th St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. (1878) *President,* M. Edward Davis. *Secretary,* Edwin J. De Costa, 720 S. Michigan Ave., Chicago 3, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. (1890) *President,* Martin Shir. *Secretary,* J. Edward Hall, 429 Clinton Avenue, Brooklyn 5, N. Y. Third Wednesday, from October to May, Kings County Medical Society, 1313 Bedford Ave., Brooklyn. N. Y.

The Obstetrical and Gynecological Society of Maryland. (1929) *President,* Emil Novak. *Secretary-Treasurer,* W. Drummond Eaton, 11 E. Chase St., Baltimore 2, Md. Meets quarterly at Maryland Chirurgical Faculty Bldg.

Cincinnati Obstetrical Society. (1876) *President,* Joseph G. Crotty. *Secretary,* Robert R. Pierce, 116 William Howard Taft Road, Cincinnati 19, Ohio. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* Rudy F. Vogt. *Secretary-Treasurer,* Glenn W. Bryant, Louisville, Ky. Meetings fourth Monday of each month from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* William Sharkey. *Secretary-Treasurer,* Jack W. Dowsett, 1020 S. W. Taylor St., Portland 5, Ore. Meetings last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. (1934) *President,* Eugene A. Conti. *Secretary-Treasurer,* David Katz, 103 Century Bldg., Pittsburgh 22, Pa. Meetings, first Monday of each month, October to May.

Obstetrical Society of Boston. (1861) *President,* Roy J. Heffernan. *Secretary,* Francis Rouillard, 1180 Beacon Street, Brookline, Mass. Third Tuesday, October to April, Harvard Club.

New England Obstetrical and Gynecological Society. (1929) *President,* Arthur E. G. Edgelow, Springfield, Mass. *Recorder,* Carmi R. Alden, 270 Commonwealth Ave., Boston 16, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. (1931) *President,* Roy E. Fallas, Los Angeles, Calif. *Secretary-Treasurer,* Donald G. Tollefson, 511 South Bonnie Brae St., Los Angeles 5, Calif.

Washington Gynecological Society. (1933) *President,* J. Bay Jacobs. *Secretary,* Allan E. King, 915 19 Street, N.W., Washington, D. C. Fourth Saturday, October, November, January, March, May.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL. The number after the Society's name is the year of founding.

New Orleans Obstetrical and Gynecological Society. (1924) *President*, Harry Meyer. *Secretary*, Abe Golden, 1430 Tulane Ave., New Orleans 12, La. Meetings held October, November, January, March, and May.

St. Louis Gynecological Society. (1924) *President*, Paul Fletcher. *Secretary*, J. Russell Vaughan, 634 North Grand Blvd., St. Louis 3, Mo., Regular meetings second Thursday, October, December, February, and April.

San Francisco Gynecological Society. (1929) *President*, Donald Dallas. *Secretary*, Donald W. de Carle, 2000 Van Ness Ave., San Francisco, Calif. Regular meetings held second Friday in month from October to April, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. (1930) *President*, S. Foster Moore. *Secretary-Treasurer*, Carey Hiett, 603 College Avenue, Fort Worth 4, Texas.

Michigan Society of Obstetricians and Gynecologists. (1924) (Formerly the Detroit Obstetrical and Gynecological Society.) *President*, O. W. Picard. *Secretary*, Carl F. Shelton, 910 David Broderick Tower, Detroit 26, Mich. Meetings first Tuesday of each month from October to May (inclusive).

Central New York Association of Gynecologists and Obstetricians. (1938) *President*, Nathan N. Cohen. *Secretary*, Merton C. Hatch, Medical Arts Bldg., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. (1940) *President*, W. N. Jones. *Secretary*, Herbert H. Thomas, 1005 South Twenty-first Street, Birmingham, Ala.

San Antonio Obstetric Society. *President*, I. T. Cutter. *Secretary*, S. Foster Moore, Jr., San Antonio, Tex. Meetings held first Tuesday of each month at Gunter Hotel.

Seattle Gynecological Society. (1941) *President*, Robert K. Plant. *Secretary-Treasurer*, Gerald F. Thomas, 1427 Medical and Dental Bldg., Seattle 1, Wash. Meetings held on third Wednesday of each month, Washington Athletic Club.

Denver Gynecological and Obstetrical Society. (1942) *President*, Edward L. Harvey. *Secretary-Treasurer*, Jack M. Simmons, Jr., 804 Republic Bldg., Denver 2, Colo. Meetings held first Monday of every month from October to May (inclusive).

Wisconsin Society of Obstetrics and Gynecology. (1940) *President*, Thomas A. Leonard. *Secretary-Treasurer*, Alice D. Watts, 324 East Wisconsin Ave., Milwaukee, Wis. Meetings held in May and October.

San Diego Gynecological Society. (1937) *President*, Clyde R. Kennedy. *Secretary-Treasurer*, John F. Wanless, 2001 Fourth Ave., San Diego 1, Calif. Meetings held on the last Friday of each month.

North Dakota Society of Obstetrics and Gynecology. (1938) *President*, W. H. Gilsdorf, Valley City. *Secretary-Treasurer*, C. B. Darner, Fargo, N. D.

Virginia Obstetrical and Gynecological Society. (1936) *President*, John M. Nokes. *Secretary*, Chester D. Bradley, 2914 West Avenue, Newport News, Va. Meetings held in April and October.

Columbus Obstetric-Gynecologic Society. (1944) *President*, Allan C. Barnes. *Secretary*, Leonard B. Greentree, 350 East Broad St., Columbus, Ohio. Meetings held last Wednesday of each month from September to May.

Naussau Obstetrical Society. (1944) *President*, Robert S. Millen. *Secretary-Treasurer*, Peter La Mariana, Williston Park, L. I., N. Y. Meetings, bimonthly from October to May.

Bronx Gynecological and Obstetrical Society. (1924) *President*, Milton D. Klein. *Secretary*. Alex Charlton, 1749 Grand Concourse, New York 53, N. Y. Meetings, fourth Monday monthly from October to May.

Washington State Obstetrical Society. (1936) *President*, E. Gerald Layton. *Secretary-Treasurer*, L. Bruce Donaldson, 805 Medical and Dental Bldg., Seattle 1, Wash. Next meeting to be held Sept. 8, 1951, Washington Athletic Club, Seattle.

Kansas City Obstetrical and Gynecological Society. (1922) *President*, Kenneth E. Cox. *Secretary*, James E. Keeler, 4301 Main St., Kansas City, Mo. Meetings last Thursday, September, November, January, and March; first Thursday, May, University Club.

Los Angeles Obstetrical and Gynecological Society. (1914) *President*, Gordon Rosenblum. *Secretary-Treasurer*, A. N. Webb, 3130 W. 6th St., Los Angeles 5, Calif.

North Carolina Obstetrical and Gynecological Society. (1932) *President*, F. Bayard Carter. *Secretary*, Richard L. Pearse, 604 W. Chapel Hill St., Durham, N. C. Meetings semiannually.

The Society of Obstetricians and Gynecologists of Canada. (1944) *President*, H. B. Atlee. *Secretary*, K. M. Grant. Annual meeting, June, 1950.

Akron Obstetrical and Gynecological Society. (1946) *President*, Alven M. Weil. *Secretary-Treasurer*, Robert M. DeWitt. Meetings held third Friday of January, April, July, and October, City Club of Akron, Ohio Bldg.

Minnesota Obstetrical and Gynecological Society. *President,* William F. Mercil. *Secretary-Treasurer,* Rodney F. Sturley, 350 Saint Peter St., St. Paul, Minn. Meetings held spring and fall.

Miami Obstetrical and Gynecological Society. (1946) *President,* John D. Milton. *Secretary,* Richard F. Stover, 701 duPont Bldg., Miami, Fla. Meetings, second Thursday in January, March, May, and November.

Omaha Obstetrical and Gynecological Society. (1947) *President,* Ralph Luikhart. *Secretary-Treasurer,* Donald C. Vroman, 813 Medical Arts Bldg., Omaha 2, Neb. Meetings held third Wednesday in January, March, May, September, November.

Oklahoma City Obstetrical and Gynecological Society. (1940) *President,* John W. Records. *Secretary-Treasurer,* Henry G. Bennett, Jr., 800 Northeast 13 Street, Oklahoma City 4.

Cleveland Obstetrical and Gynecological Society. (1947) *President,* J. L. Reycraft. *Secretary,* G. Keith Folger, 10515 Carnegie Ave. Meetings on fourth Tuesday of September, November, January, March, and May at University Club, 3813 Euclid Ave., Cleveland 15, Ohio.

New Jersey Obstetrical and Gynecological Society. (1947) *President,* Raymond T. Potter. *Secretary,* Felix H. Vann, 242 Engle St., Englewood, N. J. Meetings semiannually.

Honolulu Obstetrical and Gynecological Society. (1947) *President,* Guy C. Milnor. *Secretary,* Rodney T. West, The Clinic, Honolulu 14, T. H. Meetings third Monday of each month, Mabel Smyth Building.

Oregon Society of Obstetricians and Gynecologists. *President,* Gerald Kinzel. *Secretary-Treasurer,* Theodore M. Bischoff, 529 Mayer Bldg., Portland 5, Ore. Meetings held on third Friday of each month from October to May.

National Federation of Obstetric-Gynecologic Societies. (1945) *President,* Ralph E. Campbell. *Secretary,* Woodard D. Beacham, 429 Hutchinson Memorial Bldg., New Orleans 13, La.

Dayton Obstetrical and Gynecological Society. (1937) *President,* C. E. Mumma. *Secretary,* N. J. Thompson, 610 Harries Bldg., Dayton 2, Ohio. Meetings, third Wednesday monthly from September through June at the Van Cleve Hotel.

Dallas-Fort Worth Obstetric and Gynecologic Society. (1948) *President,* C. P. Hawkins. *Secretary,* Oran V. Prejean, 4317 Oak Lawn Ave., Dallas, Texas. Meetings in spring and fall.

Queens Gynecological Society. (1948) *President,* James, V. Rizzi. *Secretary,* George Schaefer, 112-25 Queens Blvd., Forest Hills, N. Y. Meetings held second Wednesday in February, April, October, and December, at the Queens County Medical Society Bldg.

Mississippi Association of Obstetricians and Gynecologists. (1947) *President,* John F. Lucas, Greenwood, Miss. *Secretary-Treasurer,* Claude G. Callender, 727 Carlisle St., Jackson 2, Miss. Meetings held semiannually.

Florida Obstetric and Gynecologic Society. (1948) *President,* Robert G. Spicer. *Secretary-Treasurer,* Dorothy D. Brame, 1235 Kuhl Ave., Orlando, Fla. Next annual meeting, April, 1951, at Hollywood, Fla.

South Carolina Obstetrical and Gynecological Society. (1946) *President,* John M. Fleming. *Secretary-Treasurer,* Frank B. C. Geibel, 1517 Hampton St., Columbia 1, S. C. Meetings held in spring and fall.

Buffalo Obstetrical and Gynecological Society. (1946) *President,* W. Herbert Burwig. *Secretary,* Clyde L. Randall, 925 Delaware Avenue, Buffalo, N. Y. Meetings held on the first Tuesday of October through May at the Saturn Club.

El Paso Gynecological Society. (1948) *President,* C. C. Boehler. *Secretary-Treasurer,* Robert J. Cardwell, 414 Banner Bldg., El Paso, Texas.

Kentucky Obstetrical and Gynecological Society. (1947) *President,* Clyde Sparks, Ashland, Ky. *Secretary-Treasurer,* J. B. Marshall, Louisville, Ky.

Indianapolis Obstetrical and Gynecological Society. (1947) *President,* Gerald W. Gustafson. *Secretary-Treasurer,* C. O. McCormick, Jr., 621 Hume Mansur Bldg., Indianapolis 4, Ind. Meetings held in January, April, and October.

Houston Obstetrical and Gynecological Society. (1939) *President,* Arthur Faris. *Secretary-Treasurer,* J. T. Armstrong, Hermann Professional Bldg., Houston 5, Texas. Meetings held second Tuesday of each month except July, August, and September.

Iowa Obstetric and Gynecologic Society. *President,* J. H. Randall. *Secretary,* William C. Keettel, Iowa City, Iowa.

Memphis Obstetrical and Gynecological Society. (1950) *President,* Phil C. Schreier. *Secretary,* James H. Smith, 1665 Madison Ave., Memphis 4, Tenn. Meetings, fourth Friday, October to May.

Birmingham Obstetrical and Gynecological Society. (1949) *President,* W. N. Jones. *Secretary,* Herbert H. Thomas, 1005 South Twenty-First St., Birmingham, Ala. Meetings four times yearly.

Mobile Obstetrical and Gynecological Society. (1949) *President,* John C. Hope, Jr. *Secretary,* Virginia E. Webb, 1322 Springhill Ave., Mobile, Ala. Meetings held second Thursday of January, April, July, and October.

Utah Obstetrical and Gynecological Society. (1948) *President,* William M. Nebeker. *Secretary,* Vernal H. Johnson, 2279 Jackson Ave., Ogden, Utah. Meetings held second Thursday of October, December, March, and May, at the University Club, Salt Lake City.

Inter-urban Obstetrical and Gynecological Society. (1949) *President,* D. E. Cannell. *Secretary,* E. R. Duggan, 16 North Goodman St., Rochester 7, N. Y. Next meeting will be held in Toronto, October, 1951.

New Mexico Obstetrical and Gynecological Society. (1947) *President,* Louis McRae. *Secretary-Treasurer,* LeRoy J. Bowers, Lovelace Clinic, Ridgecrest Drive and Gibson Ave., Albuquerque, N. Mex. Meetings held third Thursday in March, June, September, and December.

Pacific Northwest Obstetrical and Gynecological Association. (1947) *President,* Frank L. MacPhail. *Secretary,* Richard D. Reekie, W. 407 Riverside Ave., Spokane 8, Wash. Next annual meeting, June 25-28, 1952, Many Glaciers Hotel, Glacier Park, Montana.